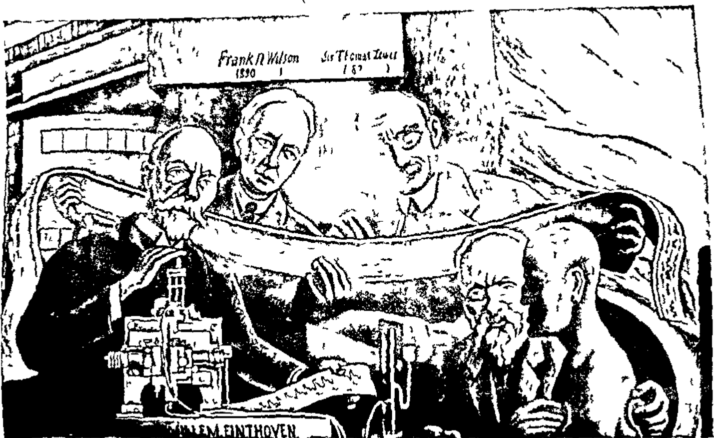


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DEDICATION TO FRANK NORMAN WILSON

by Hans H Hecht

University of Utah College of Medicine Salt Lake City Utah

On February 16 1956 a conference convened at the Barbizon Plaza Hotel in New York N Y in an attempt to bring together scientists of various disciplines who shared a common interest in the electrical manifestations of the heartbeat This conference was held under the auspices of The New York Academy of Sciences Section of Biology and of the National Heart Institute of the National Institutes of Health The present monograph records the thoughts expressed during this two-day session of formal presentations and informal discussions It does not deal with the empiricism of clinical electrocardiography but attempts to represent in cross section a branch of the natural sciences fifty years after this field had received its greatest stimulus through the introduction of the string galvanometer into physiology If this monograph succeeds in reflecting basic concepts of cardiac electrophysiology at the mid century level it will serve as a new foundation to a future electrocardiology that will be based far more on the principles of biophysics and mathematics than on empirical experimentation and experience

No one was more aware of the limitations and needs of electrocardiography than Frank Norman Wilson who from 1914 to 1952 was director of the Heart Station of the University Hospital and Professor of Medicine of the University of Michigan Ann Arbor Mich Wilson was born lived and died within a radius of a hundred miles but his ideological conceptions had a truly world wide impact He was fortunate enough to see his labors rewarded by the general acceptance of his teachings and to know they would be carried further by a small band of disciples most of whom contributed heavily to the conference on which this monograph is based There is no real beginning however as there is no real end Wilson s contribution grew from a prepared soil It is appropriate therefore to picture him in discourse with Willem Einthoven Thomas Lewis and Augustus D Waller as in the famous mural by Diego Rivera at the National Institute of Cardiology in Mexico City Even further and transcending the boundaries of a discipline one may recognize the great analyzers of the nineteenth century including Hermann von Helmholtz William Thomson Gustav Kirchhoff Max Planck and a host of others as godfathers of the ideas and statements contained in the following pages

GREETINGS FROM THE NATIONAL HEART INSTITUTE

By J. Franklin Yeager

National Heart Institute, National Institutes of Health, Public Health Service, Department of Health, Education and Welfare, Bethesda, Md.

Through recommendation of the National Advisory Heart Council, the National Heart Institute of the National Institutes of Health has had the privilege of making research grant funds available in partial support of the conference on which this monograph is based. The New York Academy of Sciences is to be congratulated upon the many fine conferences held under its sponsorship and on the ensuing publications.

We are living in an age of scientific and medical specialization that has developed to such a degree that frequently it is difficult for scientists in one area to communicate understandingly with those in other, even related, areas. Conferences such as the one resulting in this publication represent one way of helping to meet this problem. May I hope, therefore, that all readers of these pages will acquire new insights into the problems posed by the basic mechanisms of cardiac function, and that some may resume work in their laboratories with new ideas for experimental attacks upon these elusive problems.

INTRODUCTION TO PART I

by Kenneth S Cole

National Institute of Neurological Diseases and Blindness National Institutes of Health Public Health Service Department of Health Education and Welfare Bethesda Md

It is a very special privilege to introduce and to contribute to this section of the monograph and I feel very humble in being thus associated with those who know so much more about the heart than I particularly with Frank N Wilson and many of his students admirers critics and friends who are also represented in these pages

It was the late H B Williams of Columbia University New York N Y who introduced me to Wilson first in the manuscript of the monograph he wrote in collaboration with Macleod and Barker and later to Wilson in person for whom I developed an ever increasing respect and affection

When that monograph was published neurologists were busy trying to understand brain waves in terms of their experience with nerves in moist chambers and Wilson gave them a needed but not altogether painless introduction to the complications of volume conductors to which Helmholtz Einthoven and others had contributed for the benefit of electrocardiology

It is now particularly appropriate that in turn neurophysiology should offer the results of its singular good fortune and inspired hard work as suggestions and guides for the better understanding of the cellular events during the cardiac cycle The axonologist might thus be likened at the moment to the rather unpleasant rooster who rolled an ostrich egg in front of his flock and said I don t want you girls to feel I am critical or demanding but I do think that you ought to know what has been done

BEYOND MEMBRANE POTENTIALS

By Kenneth S. Cole

National Institutes of Health, Bethesda, Md.

The difference of electrical potential across the membrane of the individual cardiac muscle fiber—with its variation along the fiber and during the cardiac cycle—is a basic unit of the electrophysiology of the heart. Without adequate knowledge of this cellular unit of activity many problems of extracellular potentials could be approached only intuitively or in terms of assumed properties as was done for example by Wilson *et al.*[1] Now that the membrane potentials have become directly measurable[2] experimental ingenuity and diligence coupled with imagination and power of analysis can be expected to produce many needed and probably surprising answers. The membrane potential however, is only an intermediate step resulting from the accumulation of electrical energy and the control of its release at the membrane. The nature of these processes likewise is no longer a remote problem.

The continuing accumulation of experimental evidence[2, 3] with increasingly powerful methods and used on an ever widening number of irritable cells seems to emphasize the impressive similarities of membrane behaviors rather than the numerous individual differences. The passive electrical characteristics of most cell membranes are so strikingly uniform as to direct considerable attention to the exceptions. The magnitudes of the resting and action potentials and the various phenomena of excitation and its propagation are similar enough to suggest that the anomalies may provide the most valuable clues. To the extent that the similarities of properties and behaviors are based upon similar mechanisms any new information is of course generally applicable. For this reason the membrane of the squid giant axon[4] holds a particularly favorable—and also a particularly vulnerable—position.

Because of the size of the axon and as a result of inspired and vigorous efforts the general properties of its membrane have been described and the characteristics have been measured with a completeness that has not even been approached for any other cell membrane. The acquisition of this information can stand alone as a major achievement but what may be more important is that the data contain in themselves the necessary ingredients of the widely known and universally accepted characteristic phenomena[5, 6] of the overwhelming majority of irritable tissues. Thus the squid data constitute the initial and to date the only breakthrough into a completely new level of analysis and understanding.

Even on so favorable a cell as the squid axon the procedure has been neither obvious nor easy[7] and at present there is no simple substitute for these processes. A uniform nerve fiber may be described in terms of the partial differential equation and the equivalent circuit (FIGURE 1) in which the ionic current has for some time been the only but crucial unknown. After the elimination of longitudinal currents propagation capacity-displacement currents and the all-or-none response the ionic currents following abrupt changes of potential across the membrane were found[8] as shown in FIGURE 2. Such

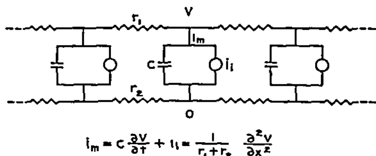


FIGURE 1 Equivalent electrical circuit and cabl equation for a single muscle or nerve fiber

ionic current data as these are, of themselves not only required in order that the axon perform its major tasks but they are also quite adequate for this purpose The corresponding information is not yet available for any cardiac membrane but it most probably constitutes the necessary first step toward any fundamental understanding

The ionic currents were then analyzed[9] into the principal components carried by sodium and potassium ions The flow of each ion was expressed as the resultant of three parameters (FIGURE 3) (1) the driving forces of its concentration ratio across the membrane—given by the equivalent electromotive forces E_N and E_K (2) the impressed potential difference and (3) the permeabilities given as conductances g_N and g_K

The conductances were found[10] to depend upon the potential difference across the membrane for both the speed and the extent of their change (FIGURE 4) for three sudden decreases of the potential difference across the membrane These characteristics embodied in Kal and Nat are the essence of the membrane properties and the points of concentration of its complexities but derived as they are from the potential step data such as are shown in FIGURE 2 they too are not yet available for cardiac or any other cell membranes

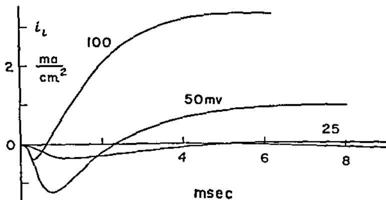


FIGURE 2 Membrane ionic currents after the indicated decreases of the membrane potential

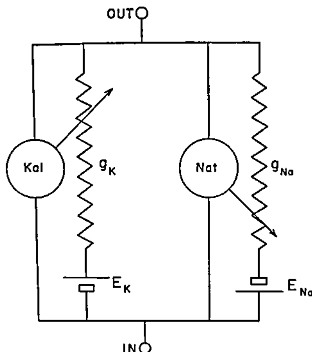


FIGURE 3 Equivalent ionic circuit with conductance controls

The ionic conductance data combined only with the axon diameter axoplasm resistivity membrane capacity and ionic potentials have been shown[10, 11] to contain to a remarkable degree the following characteristics of the squid axon (1) passive properties such as the resting resistance and rectification the anomalous inductive and capacitative reactances shown in impedance and transient

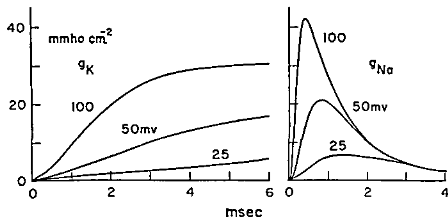


FIGURE 4 Membrane conductances after the indicated decreases of the membrane potential

measurements and ionic fluxes (2) the threshold of membrane potential for excitation the strength-duration relationship for threshold stimuli the form and amplitude of subthreshold and threshold potentials and the accommodation phenomena of utilization time and liminal gradient (3) the refractory and recovery phases and the repetitive response for continuing currents and (4) the form and amplitude of the action potential and the impedance change the velocity of propagation and the ion exchange

It is unfortunate but unfortunately true that although this impressive array of experimental data can be computed from the ionic conductances the reverse process—that is the calculation of the conductances from so many and such diverse data—has not yet been found possible

The properties of the squid axon that so completely describe so many aspects of the passive, threshold and propagation performances quantitatively are as yet not known to apply to any other cell—nor are they yet known *not* to apply If indeed the underlying mechanisms of excitation are as similar as the phenomena the properties of the squid axon ought to be available for application to cardiac problems If the processes are fundamentally different then equally adequate data must be obtained directly for cardiac membranes

It is difficult to avoid the conclusion that there can be little progress in unifying and consolidating the cardiac phenomena until an analysis of cardiac cell membrane such as has been done for the squid axon becomes possible Until then it may not be possible to know whether or not the squid data apply even qualitatively to cardiac cell membranes and to the extent they do apply what quantitative differences exist At present and perhaps until such time as similar cardiac cell characteristics are available the squid data must serve as the only guide

Obviously of course the ionic permeabilities satisfactory as they may be are themselves no more than another intermediate step They in turn need to be understood at another the molecular level and the squid axon data provide a highly specific goal and a sharp criterion of achievement Here too there has been encouraging progress but although the potassium ion conductances can be given an apparently reasonable qualitative explanation there has not been even an interesting suggestion as to the mechanism responsible for the form of the sodium conductances

Thus it appears that the squid axon data represent a correlation of electrophysiological phenomena the like of which should be vigorously sought for the cardiac cell membranes This presents an electrochemical problem the solution of which may be the all important initial step toward the understanding of the electrophysiology of the heart at about two stages beyond what is now relatively simple straightforward and commonplace

Turning to cardiac fibers I wish to emphasize that my admiration for the work of Silvio Weidmann and his colleagues is not entirely academic Although I promised him not to mention in this paper microelectrodes and other similar objects I well recall our unsuccessful attempts of twenty years ago to obtain the membrane potentials of living cardiac tissue culture cells[1] but worse than that I must also confess to having chased paramecia with a pipette

at the end of a Compton electrometer more than thirty years ago It is, therefore, very pleasant to note that Weidmann is also a contributor to these pages

References

1 WILSON F N A G MACLEOD AND P S BARKER 1933 The Distribution of the Currents of Action and of Injury Displayed by Heart Muscle and Other Excitable Tissues Univ Michigan Press Ann Arbor Mich
2 WEIDMANN S 1956 Elektrophysiologie der Herzmuskelfaser Huber Bern Switzerland
3 HODGKIN A L 1951 The ionic basis of electrical activity in nerve and muscle Biol Revs Cambridge Phil Soc 26 339–409
4 YOUNG J Z 1936 Structure of nerve fibres and synapses in some invertebrates Cold Spring Harbor Symposia Quant Biol 4 1–6
5 SCHAEFER H 1942 Elektrophysiologie Wien Deuticke
6 KATZ B 1938 Electric Excitation of Nerve Oxford Univ Press Oxford England
7 COLE K S 1955 Ions potentials and the nerve impulse *In* T Shedlovsky s Electrochemistry in Biology and Medicine Wiley New York N Y
8 COLE K S 1949 Dynamic electrical characteristics of the squid axon membrane Arch Sci Physiol 3 253–258
9 HODGKIN A L AND A F HUXLEY 1952 Currents carried by sodium and potassium ions through the membrane of the giant axon of *Loligo* J Physiol 116 449 472
10 HODGKIN A L AND A F HUXLEY 1952 A quantitative description of membrane current and its application to conduction and excitation in nerve *J Physiol* 117 500–544
11 COLE K S H A ANTOSIEWICZ & P RABINOWITZ 1955 Automatic computation of nerve excitation J Soc Ind & Appl Math 3 153–172
12 HOGG B M C M GOSS & K S COLE 1934 Potentials in embryo rat heart muscle cultures Proc Soc Exptl Biol Med 32 304–307

RESTING AND ACTION POTENTIALS OF CARDIAC MUSCLE

by Silvio Weidmann

Department of Physiology, University of Berne, Berne, Switzerland

During the second half of the past century a considerable amount of fundamental information in the field of electrophysiology was obtained by using the heart as the demonstrator organ. In 1871 Bowditch described the all-or nothing law of excitation in 1873 Engelmann *et al.* reported that the electrical force reverses its sign during excitation, in 1876 Marey established the concept of refractoriness and in 1883 Burdon Sanderson and Page obtained the first undistorted records of electrical activity by means of a capillary electrometer. The introduction of the cathode ray oscillograph deprived this tissue of its main merit its slowness and during the past few years, most of the fundamental discoveries have been made with nerve or, to be more precise with isolated fibers of *Loligo* and *Sepia*. It is no coincidence therefore that this section of the monograph has been introduced by K. S. Cole. It is my opinion that new developments in nerve physiology should serve as an incentive to those concerned with the electrophysiology of the heart.

The Ling-Gerard Electrode

A new recording technique has been one of the main factors responsible for recent progress in the field of electrophysiology.

FIGURE 1a shows a microcapillary drawn from glass tubing of about 1 mm outside diameter as described by Ling and Gerard (1949). If the tip diameter of such capillaries is well below 1 μ (FIGURE 1b) the capillaries can be made to penetrate the surface membrane of many animal cells without causing any appreciable damage. The capillaries are generally filled with a 3 M KCl solution (Nastuk and Hodgkin 1950). Their open tip leads off from the inside of a single fiber while a second electrode makes contact with the heart surface.

FIGURE 2 shows the potential changes that can be observed when a microelectrode is introduced into a spontaneously active Purkinje fiber of the dog heart. The horizontal first part of the curve was obtained with both electrodes outside the preparation (subsequently used as a zero reference potential). The microelectrode was then lowered toward a single fiber and must have entered the cell at the time marked by the first arrow. In the resting preparation the potential difference across the membrane had a value near 90 mv outside positive to inside. During activity the membrane voltage reversed the outside becoming negative to the inside. At the time marked by the second arrow the microelectrode was withdrawn from the fiber.

Movement of the tissue is a major problem in microelectrode recording. Those who have so far recorded action potentials from mammalian hearts *in situ* agree that this is a rather difficult undertaking (Woodbury *et al.* 1951, Hoffman and Suckling 1952, Trautwein and Zink 1952). New hope comes from a paper recently published by Woodbury and Brady (1956). Their method is illustrated by FIGURE 1c. An ordinary Ling Gerard electrode is

FIGURE 1 (A) Ling Gerard electrode 2.5 times natural size (B) tip of the microelectrode 55 000 times natural size—electron micrograph (Alexander and Nastuk 1953) (C) riding microelectrode leading off from inside a single fiber of a moving heart Method of Woodbury & Brady 1956

FIGURE 2 Potential changes recorded when the tip of a Ling Gerard electrode is introduced into a single Purkinje fiber of the dog heart and subsequently withdrawn

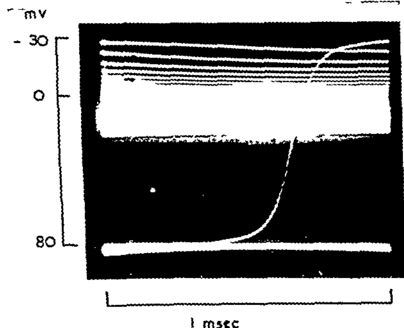


FIGURE 3 Upstroke of an action potential photographed at a sweep frequency of 1000 cyc / sec The film was exposed between the end of diastole and the height of systole Dog Purkinje fiber

cut apart (FIGURE 1a) and by means of an extremely thin wire the tip part is then connected to the amplifier input allowing the electrode to move up and down rather freely

The Shape of the Monophasic Action Potential

The upstroke of the cardiac action potential is an extremely rapid event In the ventricular conductive system of the mammalian heart it occupies only a fraction of 1 msec (FIGURE 3) In cat ventricle it takes about 1 msec (Trautwein *et al* 1954, and in the frog heart it takes a few msec (Woodbury *et al* 1951) Repolarization lasts considerably longer and the potential time course shows great variety (FIGURE 4) Ventricular muscle as a rule shows a long lasting overshoot (*a* and *b*) followed by a relatively slow return of the membrane potential to the resting level In quickly beating ventricles (rat *c*) and in auricles (*d*) the action potentials have no plateau but look triangular Records from the ventricular conductive system (*e*) show an initial 'spike and a relatively low plateau For comparison an action potential of striated muscle (rat diaphragm) is reproduced (*f*)

The Distribution of Ions

Ionic order represents stored energy Ion gradients make it possible for strong membrane currents to flow during certain phases of activity while

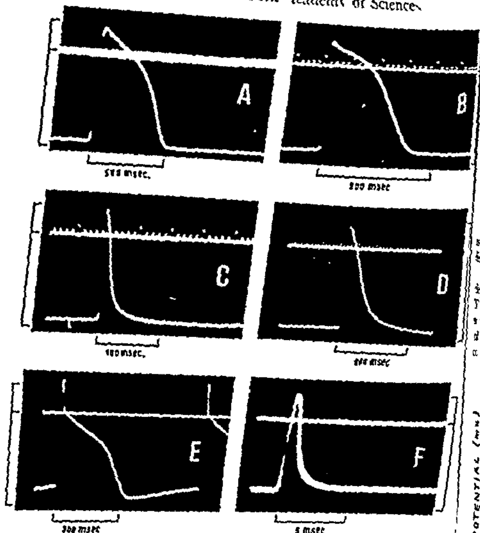


FIGURE 4. Action potentials of (A) frog heart, (B) dog ventricle, (C) rat ventricle, (D) dog auricle, (E) sheep Purkinje tissue, and (F) rat skeletal muscle. Voltage calibration: 30 mv (inside positive)–0 mv–100 mv (inside negative). From Weidmann 1956b.

metabolic energy will be required during other phases of the cardiac cycle to re-establish the ion gradients.

According to analytical data, potassium ions are accumulated in the cardiac myoplasm by a factor of about 30, while sodium ions are present at a 10 times lower concentration than in the interspace (Lowry, 1943; Robertson and Peyser, 1951; Hajdu, 1953; Krogh *et al.*, 1944; Sherrod, 1947).

Little quantitative information is available on the rate of exchange of ions between the inside of cardiac fibers and their environment. Furthermore all results so far reported are complicated by the circumstance that no distinction has been made between the turnover at rest and the increment (or decrement)

due to activity Studies made with radioactive potassium (K^+) suggest that the half time for potassium exchange must be between a few minutes and one hour (Benigno and Daudel 1950, Holland *et al* 1952, W S Wilde and J M O Brien personal communication)

Sodium ions must be extruded from the fibers against both a concentration gradient and an electrical gradient For thermodynamic reasons the postulate of a pump is a necessity However little is known about the way in which metabolic energy is used for driving this pump

Extrusion of Na^+ ions would tend to create a potential difference, and this in turn may be the cause for K^+ accumulation within the fibers (Behn 189-, Teorell 1935 Hodgkin 1951) An activity ratio of

$$K^+ \text{ inside } K^+ \text{ outside} = 30\ 1$$

is in accordance with a potential difference of 92 mv (at 37° C) a value that lies within the range of the measured resting potentials (FIGURE 5)

While potassium accumulation may well be a passive process a direct dependence of K^+ uptake on a supply of metabolic energy cannot be ruled out The problem is not without importance for heart electrophysiology a pure sodium pump (with K^+ ions moving passively) would contribute to the value of the membrane potential and some of the potential changes observed in the course of cardiac activity might be due to changes in the rate of Na^+ extrusion

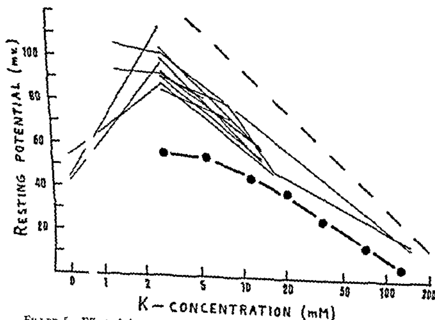


FIGURE 5 Effect of the extracellular potassium concentration (log scale) on the size of the resting potential The filled circles are values reported by Burgen and Terroux (1953) for cat auricles Other values are from Purkinje fibers of the sheep and the calf (Weidmann 1956b) The broken line indicates the theoretical slope for a membrane that is permeable exclusively to potassium ions

On the other hand if heart muscle had a coupled pump (1 Na^+ ion extruded for 1 K^+ ion absorbed) the pumping rate should have no immediate effect on the value of the membrane potential In frog skin the pump has been identified as a pure Na pump (Ussing and Zerahn 1951) In the squid giant axon both Na^+ outflow and K^+ inflow seem to depend directly on metabolism (Hodgkin and Keynes 1955) No information in this connection is available for heart muscle

Ionic Movements Underlying the Cardiac Action Potential

Electrical evidence suggests that the surface membrane of resting cardiac fibers is permeable predominantly to potassium ions Thus an increase of the extracellular K^+ concentration lowers the resting potential (FIGURE 5) while a change of the Na^+ or Cl concentration has no appreciable influence

During activity in order to change the potential difference between inside and outside an electric charge must be displaced across the fiber membrane (Hodgkin and Huxley 1952b Cole elsewhere in this publication)

In heart as in squid nerve the upstroke of the action potential seems to be due to a permeability increase of the surface membrane to Na^+ ions allowing positive charge to enter the fiber at a high rate The evidence for this view is as follows

(1) Heart muscle fails to conduct when more than 90 per cent of the extracellular NaCl is replaced by isosmotic sucrose (Overton 1902)

(2) With an activity ratio of

$$Na^+ \text{ inside } Na^+ \text{ outside} = 1\ 10$$

an *exclusively* sodium permeable membrane should be the seat of a potential

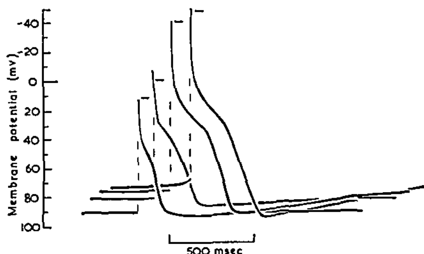


FIGURE 6 Effect of sodium concentration on the size and shape of action potential Kid Purkinje fiber The extracellular sodium content was (from left to right) 13 22 100 and 150 per cent of the normal The horizontal lines indicate expected changes in the height of action potentials if membrane is assumed to be exclusively permeable to sodium ions

difference of 61 mv inside positive to outside The value of the reversed potential difference at the beginning of the action potential approaches this sodium equilibrium potential but does not reach it

(3) Replacing part of the extracellular NaCl by sucrose or adding solid NaCl to the bathing solution has no appreciable effect on the size of the resting potential (FIGURE 6) The height of the action potential however is affected as if (during the crest of the spike) the membrane were predominantly permeable to Na^+ ions (Cranefield *et al* 1953 Draper and Weidmann 1951)

(4) At the crest of the initial spike the membrane resistance of a Purkinje fiber is lowered to about 1 per cent of its diastolic value suggesting an increase in ionic permeability (FIGURE 7)

Little is known about the ionic movements that are responsible for repolarization In the case of Purkinje fibers the descending limb of the initial spike may be due to a decrease in Na^+ permeability This is suggested by the finding that the membrane resistance increases during that phase of the action potential (FIGURE 7) The question why there is no rapid repolarization as in nerve and muscle can probably be answered thus when Purkinje fibers are depolarized for several seconds by external current their membrane resistance does not undergo any large decrease (Weidmann 1951b) This is contrary to the behavior of squid nerve (Hodgkin and Huxley 1952b) or frog skeletal muscle (Jenerick 1953) and suggests that the K^+ permeability in cardiac muscle does not rise to any considerable extent as a consequence of depolarization It becomes difficult then to explain why the membrane repolarizes at all This problem will be taken up again later in this paper

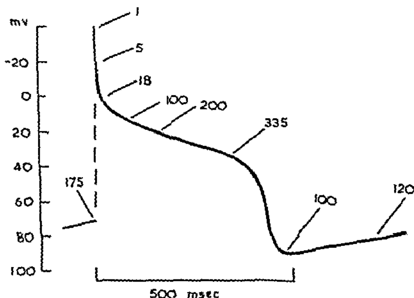


FIGURE 7 Change of membrane resistance during electrical activity Kid Purkinje fiber The figure attached to the curve indicate membrane resistance in relative units Redrawn from Weidmann 1951

Wilde and O Brien (1953) recently succeeded in showing that each action potential of a turtle ventricle is associated with a relatively large discharge of K^+ from the fibers into the vascular bed This result might be expected on the grounds of electrical data During the action potential the electrical force tending to keep K^+ ions inside the cell disappears allowing K^+ ions to flow down their concentration gradient It should be stressed at this point that the finding of an increased K^+ outflow during activity does not necessarily signify an increased permeability of the surface membrane to K^+ ions The increase in flow may be due wholly to an increase of the driving force (Teorell 1949)

From the results of Wilde and O Brien (1953) it must be assumed that the K^+ concentration of the interspace rises toward the end of the action potential From the work of Yoshida (1926) it is known that the application of K^+ rich solution to a frog heart shortens its monophasic action potential The question then is asked whether in the course of the normal heartbeat the increase of the extracellular potassium concentration may be responsible for initiating repolarization (*Weidmann 1956a*)

Again the slowly beating turtle ventricle makes it possible to test this hypothesis At 10° C its action potential has a duration of 3 to 5 sec while substances admixed to the coronary perfusate reach the heart muscle fibers with a delay of the order of 1 sec making it possible to change the extracellular solution in the course of a single action potential In the experiment illustrated in FIGURE 8 an action potential was first photographed under normal perfusion

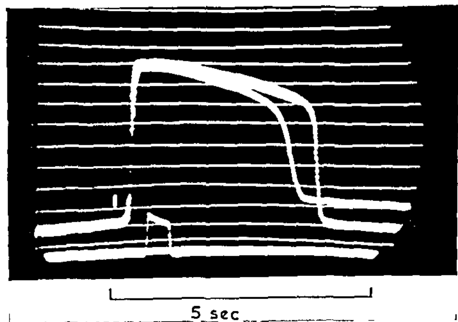


FIGURE 8 Shortening of the cardiac action potential due to an injection of KCl into the coronary circulation of a turtle heart The moment of injection is marked on the lowest trace Voltage calibration lines from 10 to 10 mv

conditions. During a second sweep cycle a slug of K^+ rich solution was made to enter the coronary artery at a time when a second action potential had already started. This resulted in an earlier and incomplete repolarization, suggesting that a high K concentration has a double action: repolarization of an active fiber and depolarization of a resting fiber.

The action of K^+ ions on resting fibers can be explained on the assumption that the ratio inside K^+ : outside K^+ largely determines the value of the resting potential (FIGURE 5). The effect of K^+ ions on active fibers is contrary to that predictable from the equations of a diffusion potential (Goldman, 1943; Hodgkin, 1951). Therefore the repolarizing effect of K^+ ions must be explained in some more complicated way, for example (1) stimulation of active Na^+ extrusion, (2) a decrease of the Na^+ permeability and therefore of Na^+ inward current, or (3) a mild increase of the K^+ permeability and therefore of K^+ outward current.

The hypothesis that the rising extracellular K^+ concentration outside the excitable membranes serves as a "signal" for repolarization seems attractive

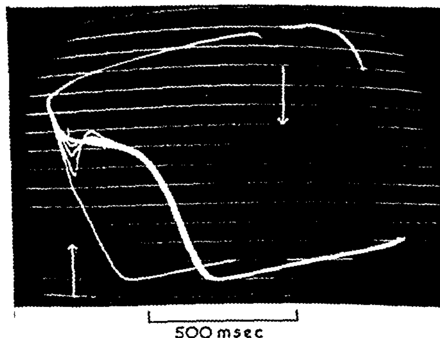


FIGURE 9. Plateau of action potential at a semistable level. Kid Purkinje fiber. action potentials superimposed by synchronizing flyback of sweep circuit with u... tion potential. Electric current was turned on during the spike of the action p... (arrow pointing downward) and switched off in the beginning of the plateau (arrow upward). Relative current strengths 1, 2, and 3 were subthreshold. Strength 4 ... the action potential off. Voltage calibration lines from 10 to 10 mv.

but cannot be pressed Quantitative arguments suggest that a sufficiently high K^+ concentration could be reached only if the e caping ions met a second diffusion barrier close to the excitable membrane leading to K^+ accumulation in a relatively small space

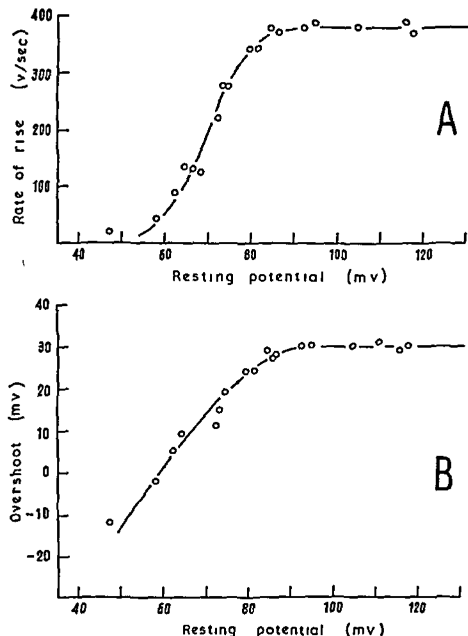


FIGURE 10 Effect of the resting potential on the rate of ri e (A) and the overshoot (B) of the action potential Sheep Purkinje fiber From Weidmann 1956b

The Phenomenon of "All or Nothing" Repolarization

In the experiment illustrated in FIGURE 9 pulses of anodal current were passed through the surface membrane of a Purkinje fiber (Weidmann, 1951). Relatively weak currents resulted in electrotonic potential changes and following the break of such weak currents the action potential followed its usual course. With a stronger current, however, it was possible to terminate the action potential—the membrane potential returned to the diastolic level even though the polarizing circuit had been broken.

In 1884 Biedermann described a phenomenon that is probably the mechanical consequence of "all or nothing" repolarization. He closed a polarizing circuit during early systole, the anode touching the surface of a frog heart. This resulted in relaxation around the anode and, if the current was strong enough, in a spread of relaxation across the surface of the contracted ventricle.

It will not be an easy task to decide whether the normal process of repolarization is a propagated phenomenon. The hypothesis is attractive since such a mechanism would provide for a synchronous end of electrical (and probably

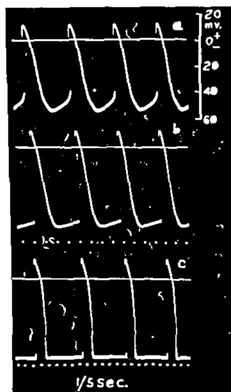


FIGURE 11. Action potentials from different regions of the same frog heart. (a) pacemaker region of the sinus venosus, (b) nonpacemaker region of the sinus venosus, and (c) auricle. From Hutter & Trautwein, 1956.

mechanical) activity in the whole ventricle the region with the largest tendency to repolarize triggering off the other parts (see pp 932-941 of this publication)

The Influence of the Resting Potential on the Upstroke Velocity and Crest Height of the Action Potential

With squid nerve Hodgkin and Huxley (1952a) made the finding that a low resting potential is associated with a low Na^+ inward current during activity FIGURE 10 shows the results of similar experiments carried out with a Purkinje fiber of the sheep Two Ling Cerard electrodes one of which was used to record the inside potential were inserted into the same fiber With the help of a feedback amplifier current could be passed through the second electrode so as to keep the membrane resting potential at a predetermined level At the

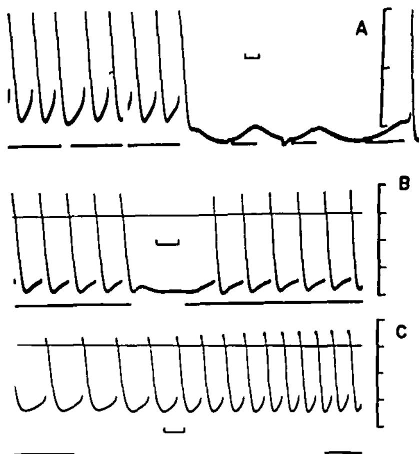


FIGURE 12 Effect of vagus and sympathetic stimulation on pacemaker potentials in the sinus venosus of the frog heart (A and B) vagi stimulated during break in lower trace and (C) vagosympathetic stimulation in an atropinized heart Voltage calibration in 20 mv steps Time 1 second From Hutter & Trautwein 1955

end of a clamp period lasting for about 100 msec the fiber was stimulated If the resting potential was kept above 90 mv (FIGURE 10) the upstroke velocity and the height of the overshoot were maximal Lower resting potentials resulted in lower rates of rise and lower overshoots until with a resting potential of about 50 mv the fibers were unexcitable It was assumed by Hodgkin and Huxley (1952b) that low resting potentials inactivate the sodium transport mechanism so that it cannot be made available to carry Na^+ ions when the membrane is rapidly depolarized

Whatever the explanation the finding is of some importance to those who investigate the effect of ions and drugs on the different parameters of the action potential Thus the decrease of the overshoot observed with K^+ rich solutions was found to be entirely due to the decrease of the resting potential (Weidmann 1955a) This became clear when by means of external current the resting potential was brought back to its original level and the overshoot then reached its original size in spite of the high extracellular K^+ concentration

Pacemaker Potentials

FIGURE 11 shows action potentials as recorded from different regions of the frog heart Record *c* is typical for the auricle or ventricle in that the resting potential stays constant during diastole Record *b* shows some slow depolarization (prepotential Arvanitaki 1938) that suggests the presence of pacemaker properties Record *a* shows an additional feature an upward convex part of the curve starting about 100 msec before the upstroke of the action potential and giving the impression of a gradual transition from rest to activity

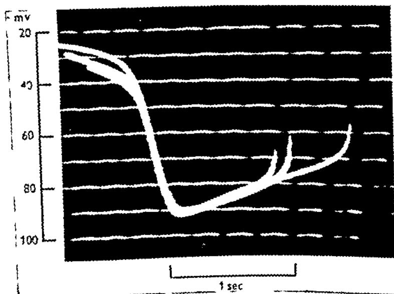


FIGURE 13 Effect of calcium ions on pacemaker potentials Records superimposed on phase of repolarization Same sheep Purkinje fiber in Tyrode solution containing 1/4 1 and 4 times the normal amount of $CaCl_2$ From Weidmann 1955b

Such curves can be obtained only in limited areas of pacemaker regions that is in the part that fires first (Bozler 1943 Brady and Hecht, 1954 del Castillo and Katz 1955 Hutter and Trautwein 1955)

Being able to record these prepotentials we thought it would be of interest to learn in what way they would be changed under the influence of such agents as are known to alter the cardiac frequency

FIGURES 12a and 12b show the effect of vagus stimulation on the sinus venosus of the frog heart A short series of stimuli (10 sec) when applied during diastole decreased the slope of the prepotential and more time was thus required to reach the firing level (the value at which the membrane potential becomes unstable) Sympathetic stimulation had the opposite effect (FIGURE 12c) that is the slope of the prepotential was increased Prolonged vagus stimulation as seen later in FIGURE 12a not only decreased the slope of the pre potential but led to hyperpolarization thereby preventing the pacemaker from firing (Gaskell effect Gaskell 1887)

A different way of influencing the cardiac frequency is illustrated in FIGURE 13 Here the calcium content of the bathing solution was varied This re sulted in no appreciable change of the resting potential nor was the initial slope of the prepotential affected An increase of the calcium concentration how ever shifted the firing level away from the resting potential resulting in a lower cardiac frequency or even cardiac standstill

References

ALEXANDER J T & W L NASTUK 1953 An instrument for the production of micro electrodes used in electrophysiological studies Rev Sci Instr 24 528-531

ARVANITAKI A 1938 Propriétés rythmiques de la matière vivante II Étude expéri mentale sur le myocarde d *Helix* Hermann Paris France

BEHN U 1897 Über wechselseitige Diffusion von Electrolyten in verdünnten wässerigen Losungen insbesondere uber Diffusion gegen das Konzentrationsgefälle Ann Phys Chem Neue Folge 62 54-67

BENIGNO P & P DAUDEL 1950 Radio potassium et coeur isolé de grenouille I Le partition du potassium entre l organe et le liquide de Ringer J Physiol Paris 42 233-242

BIEDERMANN W 1884 Beiträge zur allgemeinen Nerven und Muskelphysiologie 14 Mitteilung Über das Herz von *Helix pomatia* Sitzber Kais Akad Wiss Math naturw Kl 89 19-55

BOWDITCH H P 1871 Über die Eigenthümlichkeiten der Reizbarkeit welche die Muskel fasern des Herzens zeigen Ber Verhandl K sachs Ges Wiss Math phys Kl 23 652-689

BOZLER F 1943 The initiation of impulses in cardiac muscle Am J Physiol 138 273-282

BRADY A J & H H HECHT 1954 On the origin of the heart beat Am J Med 17 110

BROOKS C McC B F HOFFMAN F E SUCKLING & O ORIAS 1955 Excitability of the Heart Grune and Stratton New York N Y

BURDON SANDERSON J & F J M Page 1883 On the electrical phenomena of the excitatory process in the heart of the frog and of the tortoise as investigated photographically J Physiol London 4 327-338

BURGEN A S V & K G TERROUX 1953 On the negative inotropic effect in the cat s auricle J Physiol London 120 449-464

CRANEFIELD P F J A E EYSTER & W F GILSON 1951 Effect of reduction of external sodium chloride on the injury potentials of cardiac muscle Am J Physiol 166 269-272

DEL CASTILLO J & B KATZ 1955 Production in membrane potential changes in the frog heart by inhibitory nerve impulses Nature 175 1035

DRAPER M H & S WEIDMANN 1951 Cardiac resting and action potentials recorded with an intracellular electrode J Physiol London 115 74–94

ENGELMANN NUEL & PEKELHARING 1873 Over de electromotorische verschijnselen van het hart Konink1 Ned Acad Wetenschap Proc June 28 2–3

GASKELL W H 1887 On the action of muscarin upon the heart and on the electrical changes in the non beating cardiac muscle brought about by stimulation of the inhibitory and augmentor nerves J Physiol London 8 404–415

GOLDMAN D E 1943 Potential impedance and rectification in membranes J Gen Physiol 27 37–60

HAJDU S 1953 Mechanism of staircase and contracture in ventricular muscle Am J Physiol 174 371–380

HODGKIN A L 1951 The ionic basis of electrical activity in nerve and muscle Biol Revs Cambridge Phil Soc 26 339–409

HODGKIN A L & A F HUXLEY 1952a The dual effect of membrane potential on sodium conductance in the giant axon of *Loligo* J Physiol London 116 497 506

HODGKIN A L & A F HUXLEY 1952b A quantitative description of membrane current and its application to conduction and excitation in nerve J Physiol London 117 500–544

HODGKIN A L & R D KEYNES 1955 Active transport of cations in giant axons from *Sepia* and *Loligo* J Physiol London 128 28–60

HOFFMAN B F & E E SUCKLING 1952 Cellular potentials of intact mammalian hearts Am J Physiol 170 357–362

HOLLAND W C C E DUNN & M E GREIG 1952 Studies on permeability VIII Role of acetylcholine metabolism in the genesis of the electrocardiogram Am J Physiol 170 339–345

HUTTER O F & W TRAUTWEIN 1955 Effect of vagal stimulation on the sinus venosus of the frog s heart Nature 176 512 513

HUTTER O F & W TRAUTWEIN 1956 Vagal and sympathetic effects on the pacemaker fibers in the sinus venosus of the heart J Gen Physiol 9 715–733

JENERICK H P 1953 Muscle membrane potential resistance and external potassium chloride J Cellular Comp Physiol 42 427–448

KROGH A A L LINDBERG & B SCHMIDT NIELSEN 1944 The exchange of ions between cells and extracellular fluid II The exchange of potassium and calcium between the frog heart muscle and the bathing fluid Acta Physiol Scand 7 221–237

LING G & R W GERARD 1949 The normal membrane potential of frog sartorius fibers J Cellular Comp Physiol 34 383–396

LOWRY O H 1943 Electrolytes in the cytoplasm Biol Symposia 10 233–245

MAREY E J 1876 De excitations électriques du coeur *In* Physiologie expérimentale Travaux du Laboratoire de M Marey 2 63 Masson Paris France *Quoted by* Brooks *et al* 1955

NASTUK W L & A L HODGKIN 1950 The electrical activity of single muscle fibers J Cellular Comp Physiol 35 39 73

OVERTON E 1902 Beiträge zur allgemeinen Muskel und Nervenphysiologie Pflügers Arch ges Physiol 92 346–386

ROBERTSON W VAN B & F PEYSER 1951 Changes in water and electrolytes of cardiac muscle following epinephrine Am J Physiol 166 277–283

SHERROD T R 1947 Effects of digitalis on electrolytes of heart muscle Proc Soc Exptl Biol Med 65 89–90

TEORELL T 1935 Studies on the diffusion effect upon ionic distribution I Some theoretical considerations Proc Natl Acad Sci U S 21 152 161

TEORELL T 1949 Permeability Ann Rev Physiol 10 545–564

TRAUTWEIN W U GOTTSTEIN & J DUDEL 1954 Der Aktionsstrom der Myokardfaser im Sauerstoffmangel Pflügers Arch ges Physiol 260 40–60

TRAUTWEIN W & K ZINK 1952 Über Membran und Aktionspotentiale einzelner Myokardfasern des Kalt und Warmblüterherzens Pflügers Arch ges Physiol 256 68–84

USSING H H & K ZERAHN 1951 Active transport of sodium as the source of electric current in short circuited isolated frog skin Acta Physiol Scand 23 110–127

WEIDMANN S 1951 Effect of current flow on the membrane potential of cardiac muscle J Physiol London 115 227–236

WEIDMANN S 1955a The effect of the cardiac membrane potential on the rapid availability of the sodium carrying system J Physiol London 127 213–224

WEIDMANN S 1955b Effects of calcium ions and local anaesthetics on electrical properties of Purkinje fibres J Physiol London 129 568–582

WEIDMANN S 1956a Shortening of the cardiac action potential due to a brief injection of KCl following the onset of activity J Physiol London 132 157–163
WEIDMANN S 1956b Elektrophysiologie der Herzmuskelfaser Huber Bern Switzerland and Stuttgart Germany
WILDE W S & J M O BRIEN 1953 The time relation between potassium (K^{42}) outflux action potential and the contraction phase of heart muscle as revealed by the effluogram Abstr 19th Internat Physiol Congr 889–890 (See Wilde s paper in this monograph pp 693–699)
WOODBURY J W & A J BRADY 1956 Intracellular recording from moving tissues with a flexibly mounted ultramicroelectrode Science 123 100–101
WOODBURY J W & A J BRADY 1956 A flexibly mounted ultramicroelectrode for intracellular recording from moving tissues Science 123 In press
WOODBURY L A H H HECHT & A R CHRISTOPHERSON 1951 Membrane resting and action potentials of single cardiac muscle fibers of the frog ventricle Am J Physiol 164 307–318
YOSHIDA H 1926 Zur Deutung des Elektrokardiogramms I Das Elektrogramm der Ventrikelspitze des Froschherzens Z Biol 84 51–78

SOME MOLECULAR ASPECTS OF HEART BEHAVIOR

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The heart cycle is conveniently thought of as beginning with the excitation of the pacemaker cells in the sinoauricular node Beginning here the wave of electrical depolarization spreads over the auricles and finally over the ventricles Depolarization sets off the muscular contraction of the auricles then of the ventricles This period of systole ordinarily lasts about 0 4 sec and the cycle is completed by a rest period of approximately equal length the diastole Difficulties such as flutter fibrillation and congestive heart failure are disorganizations that arise because of changes in the individual heart cells

The cell with its nucleus and cytoplasm is surrounded by a membrane about 100 A thick The proteins and fatty materials such as lecithin are packed in an orderly fashion with no unfilled holes that might contribute to thermodynamic instability The observed tendency of simple proteins to coil into spirals may be expected to manifest itself also in the proteins of the membrane unless awkward side groups interfere Protein spirals consisting of 21 to 30 amino acids as in insulin presumably sit like so many upright barrels upon a layer of fatty material that rests in its turn on a second layer of upright barrel like protein spirals to form the sandwichlike structure of the membrane In general the spirals are oriented so that the amino endgroups with their positive charges are directed toward the negative charge in the cytoplasm while the negative carboxyl end of the barrel is directed toward the positively charged cell exterior As long as a potential in excess of the critical threshold is maintained across the membrane it will be held in this orderly resting α structure However whenever the potential falls below the threshold value the barrels presumably tip over and orient themselves so that the positive end of one barrel is against the negative end of a neighbor

This reorganized membrane with its protein molecules in the state called supercontracted in contracted muscle or in shrunken wool is markedly more permeable than the membrane in its resting state As a result there is an inward rush of sodium ions reversing the direction of the membrane potential and the membrane enzymes are now more accessible to the substrate Consequently the onset of this permeable state initiates a period of marked chemical activity in which there is formed a metabolite that finally pumps out the excess sodium that had entered the cell at the beginning of the action phase With the restoration of the resting potential the cell structure again resumes the resting state However before the comparatively slow manufacture of metabolic pump substance makes much headway in expelling the excess sodium the potassium that is no longer held by the resting potential and is about 45 times as concentrated inside the cell as outside begins diffusing out through the permeable supercontracted membrane and thus sparks the trend back toward the resting state

One can scarcely exaggerate the importance of this outwardly directed po

tassium current in contributing to the restoration of the resting state With out the outward potassium current excessive elaboration of sodium pump substance would be required to restore the resting state, and this would drain the cell's resources Certain naturally occurring substances such as acetyl choline in cholinergic cells and, possibly norepinephrine in adrenergic cells increase this outward potassium current by increasing the membrane perme ability to potassium This speeds up the initial stages of the return to the resting state Restoration is finally completed by the outward pumping of the sodium ion This sodium pumping results from a union of sodium with a metabolically formed pump substance *P* to form NaP^+ inside the cell This NaP^+ readily permeates the membrane and being much more concentrated inside the cell than outside finally gives a strong outward positive sodium current that restores the resting potential Undoubtedly contributions of other lesser ion currents will be identified in the future In recovering the resting state some cells overshoot the resting potential The excess pump substance formed during the active state while the membrane enzymes were accessible causes the outward NaP^+ current to build up an exces of positive *charge outside the cell This excess potential present at the beginning of the* resting state, then decays because of an inward potassium current as well as a drop in NaP^+ concentration inside the cell this is due to a slowing of the production of P as the enzymes in the membrane become less accessible to sub strate In the pacemaker cells the drop in positive charge outside the recov ered cells carries the transmembrane potential below the threshold value and this restarts the entire cycle

This spontaneous firing can be brought on in any type of cell by a lessening of the stability of the resting membrane structure that is by shifting the thresh old potential by adsorbing appropriate types of molecules Thus the mole cules we smell through our noses in effect transform our nasal end organs into pacemaker cells with spontaneous repetitive firing The intensity of the odor perceived is roughly proportional to the frequency with which the nerves fire This sort of lessening of membrane stability in the heart cells by drugs or by any other causes may result in the firing of scattered cells ahead of the usual pacemakers Depolarization spreading from such ectopic centers may pass through the whole heart and introduce an extra beat that will be wasteful and inefficient if the chambers of the heart have not had time to fill with blood since the previous beat A more serious situation arises when the spreading depolarization from an ectopic center is deflected from sections of the heart that are still refractory not yet having recovered excitability from the last beat with the result that the wave of excitation follows a circuit in which only a fraction of the heart is excited Depending on the number of such independent circuits and the consequent lack of muscular coordination the heart is said to flutter or to be in a state of fibrillation Only simultaneous depolarization of the whole heart by ma sive electric shock or by temporary stoppage of the heart by chemical means as by bathing it with strong KCl can restore an orderly depolarization dominated by the normal pacemakers in the sinoauricular node

Single-Cell Membrane Permeability

As previously noted a single cell consists of a complex membrane separating two salt solutions of different composition Because of selective permeability to sodium and other ions a potential is developed across the membrane and in turn this potential makes possible the selectivity The total behavior of the cell in its environment is determined very specifically by the changes in the permeability and in the associated alterations of potential as the cell passes from the resting state to the active phase

From the point of view of relaxation or rate theory, the simplest model of a cell membrane that will reproduce the observed behavior may be described as follows[14] without needing to specify in detail the chemical structure of the cell wall we suppose that there are a number (perhaps ten to twenty) of potential energy barriers to molecular transport each minimum of which is characterized by a molecular population and each maximum by an activation free energy for transport In the absence of diffusing molecules or ions the relative heights of these maxima may be presumed to be more or less arbitrarily distributed but when a flux of charged species is present the apparent free energy differences between successive maxima probably becomes very nearly constant a higher barrier will tend to be lowered by the potential of the ions trapped behind it while a low barrier will be unaffected

Assuming such a linear decrease in the heights of the free energy maxima the equation for the steady transport of the *ith* ionic species may be written in the form

$$Q = \frac{\lambda_0 k_0^0 g}{n} \left\{ x^{-n/2} c_0 - \frac{\lambda}{\lambda_0} x^{n/2} c \right\} \qquad (1)$$

where the subscript zero refers to one side of the membrane and n to the other The λ s are the average distances between potential energy maxima k_0^0 is the reaction rate constant for the first barrier in the absence of any transmembrane potential and n is the number of barriers The quantity g is a correction term that we shall generally take as unity Finally c is the concentration of the species and x is defined as

$$x = \exp\ (z \mathfrak{F} \mathcal{E}/n\mathrm{RT}) \qquad (1a)$$

where z is the charge on the *ith* ion (with sign) and $\mathcal{E}$ is the transmembrane potential difference

From this equation we see that the flux of any species depends on three principal factors (1) the permeability $\mathrm{P} = \lambda_0 k_0^0 g/n$ (2) the concentration difference across the membrane and (3) the activity coefficients $\exp \pm (z\mathfrak{F}\mathcal{E}/2\mathrm{RT})$ giving the electrical driving force on an ion To a first approximation the permeability depends on the nature and thickness of the membrane (λ_0 the length of a jump and n the number of barriers) and on the rate at which the ion traverses the first barrier in the absence of an electrical field On the other hand the activity coefficients depend primarily on the electrical propertie of the system that is on the potential across the membrane and the number of charges on the ion

tassium current in contributing to the restoration of the resting state. Without the outward potassium current, excessive elaboration of sodium pump substance would be required to restore the resting state and this would drain the cell's resources. Certain naturally occurring substances such as acetylcholine in cholinergic cells and possibly norepinephrine in adrenergic cells increase this outward potassium current by increasing the membrane permeability to potassium. This speeds up the initial stages of the return to the resting state. Restoration is finally completed by the outward pumping of the sodium ion. This sodium pumping results from a union of sodium with a metabolically formed pump substance P to form NaP^+ inside the cell. This NaP^+ readily permeates the membrane and, being much more concentrated inside the cell than outside, finally gives a strong outward positive sodium current that restores the resting potential. Undoubtedly contributions of other lesser ion currents will be identified in the future. In recovering the resting state some cells overshoot the resting potential. The excess pump substance formed during the active state while the membrane enzyme were accessible causes the outward NaP^+ current to build up an excess of positive charge outside the cell. This excess potential present at the beginning of the resting state then decays because of an inward potassium current as well as a drop in NaP^+ concentration inside the cell; this is due to a slowing of the *production of P as the enzymes in the membrane become less accessible to substrate*. In the pacemaker cells the drop in positive charge outside the recovered cells carries the transmembrane potential below the threshold value and this restarts the entire cycle.

This spontaneous firing can be brought on in any type of cell by a lessening of the stability of the resting membrane structure, that is, by shifting the threshold potential by adsorbing appropriate types of molecules. Thus the molecules we smell through our noses in effect transform our nasal end organs into pacemaker cells with spontaneous repetitive firing. The intensity of the odor perceived is roughly proportional to the frequency with which the nerves fire. This sort of lessening of membrane stability in the heart cells by drugs or by any other causes may result in the firing of scattered cells ahead of the usual pacemakers. Depolarization spreading from such ectopic centers may pass through the whole heart and introduce an extra beat that will be wasteful and inefficient if the chambers of the heart have not had time to fill with blood since the previous beat. A more serious situation arises when the spreading depolarization from an ectopic center is deflected from sections of the heart that are still refractory, not yet having recovered excitability from the last beat, with the result that the wave of excitation follows a circuit in which only a fraction of the heart is excited. Depending on the number of such independent circuits and the consequent lack of muscular coordination the heart is said to flutter or to be in a state of fibrillation. Only simultaneous depolarization of the whole heart by massive electric shock or by temporary stoppage of the heart by chemical means, as by bathing it with strong KCl, *can restore an orderly depolarization dominated by the normal pacemakers in* the sinoauricular node.

Single Cell Electrograms and the Electrocardiogram

In the method developed by Ling and Gerard, a hollow glass electrode less than 1 μ thick and filled with KCl solution is inserted through the membrane into the interior of a cell with the second electrode outside. An electrogram similar to the one shown in FIGURE 1 is the result. The potential difference is measured between the inside and the outside of the cell membrane.

We shall now outline briefly the standard calculation of potential V at an electrode due to a miscellaneous collection of membranes, each a leaky condenser, such as are present in the heart. We first consider the potential δV at a point a distance r from the center of the near plate of a condenser. The condenser is composed of 2 parallel plates a distance d apart, each of δA area and carrying a uniform charge σ per square centimeter. θ measures the angle between the normal to the near plate and the vector from the electrode to the center of the near plate (FIGURE 2). We must then have

$$\delta V = \frac{\delta A\sigma}{\epsilon}\left\{\frac{1}{r} - \frac{1}{r_1}\right\} = \frac{r^2\delta\omega\sigma d}{\cos\theta\ \epsilon}\left\{\frac{1}{r} - \frac{1}{[r^2 + 2rd\cos\theta + d^2]^{\frac{1}{2}}}\right\} \tag{3}$$

$$= \frac{\sigma d\delta\omega}{\epsilon}$$

We have written $\delta\omega$ for the solid angle subtended by surface δA about the electrode. For a collection of such condensers we have the potential

$$V = \sum(\delta V) = \sum\frac{\sigma\ d\ \delta\omega}{\epsilon} \tag{4}$$

If an electrode is removed far enough from a collection of finite condensers each solid angle $\delta\omega$ vanishes so that the potential V must vanish. Such a neutral electrode with the potential $V = 0$ is realized approximately following Wilson by connecting 3 leads attached to the 2 arms and the left leg. The 3 leads are joined by wires of 5000 ohms resistance to form the single neutral

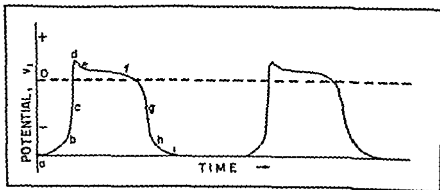


FIGURE 1. Single cell action potential.

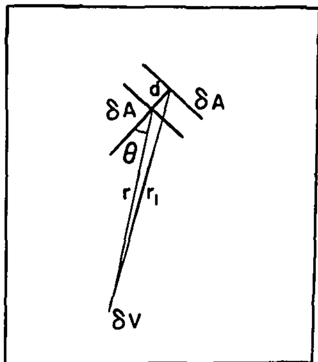


FIGURE 2 Potential due to a condenser

electrode The potential difference between the neutral electrode and an exploring electrode is thus given by EQUATION 4 Let us apply EQUATION 4 in the calculation of the potential difference between the inside and the outside of a cell carrying a uniform charge of magnitude $|\sigma|$ over its surface For a point outside the cell we have $i = 0$ since $\sum \delta\omega = 0$ For a point inside the resting cell $i = -\frac{4\pi|\sigma|d}{\epsilon}$ since we have $\sum \delta\omega = 4\pi$ and the surface density of the charge on the inside surface of the resting cell membrane is $-|\sigma|$ Thus the external resting potential of the cell is higher than the internal by $\frac{4\pi|\sigma|d}{\epsilon}$ or in general we have for this relative external potential for the ith cell surface

$$v = \frac{4\pi\sigma d}{\epsilon} \tag{5}$$

In general if σ is the charge on the side of the membrane nearest the probing electrode we have

$$\sigma = \frac{\epsilon v}{4\pi d} \tag{6}$$

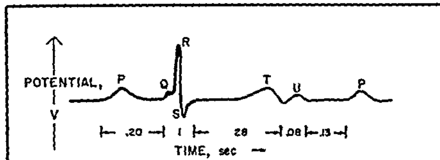


FIGURE 3 Electrocardiogram VF The neutral electrode following Wilson is a triple connection to the 2 arms and the left leg with 5000 ohms resistance between each of the leads The exploring electrode is placed on the left leg [7]

Substituting EQUATION 6 in EQUATION 3 gives, for the potential V at the probing electrode (FIGURE 3) in terms of the v across the ith segment

$$V = \sum v_i \frac{\delta\omega_i}{4\pi} \qquad (7)$$

Here one totals up all the membrane segments in the heart For each membrane segment one needs to know the solid angle it subtends and its phase in the cycle Knowing the phase, one can read v from the appropriate cell diagram illustrated in FIGURE 1

In the resting state of the heart the sum of $\delta\omega$ over membrane segments having a potential $+v$ is just equal to the sum of the solid angles with $-v$ so that $V = 0$ wherever the exploring electrode is situated Suppose we place our electrode just over the part of the ventricle where polarization starts As polarization begins to spread we can calculate with reasonable approximation the potential contributions from only the membrane at the interface between the resting and the excited region This is because the potential contribution inside the resting region cancels out while the contribution inside the excited region approximately cancels except around the boundary Integrating over the surface of the excited region one assigns a value of zero to an area newly excited while if depolarization has been going on for a length of time t the appropriate potential may be deduced from FIGURE 1 by choosing the v corresponding to the appropriate value of t It is evident that only the boundaries of the excited region that have stopped advancing by coming to the end of excitable tissue as at the heart s surface, will contribute to the potential V Now V at the beginning of excitation will start increasing approximately proportional to v until the excitation wave reaches the far side of the heart when the difference between the out-of phase v values will cause V to increase more like the first derivative Actually depending on the phase relations on the surface of excitation region V may increase like higher derivatives of the cell potential v Since V mirrors the changes in v one can only hope to arrive at a fundamental understanding of electrocardiography through a clear understanding of single-cell potentials

Acknowledgments

We express our appreciation for helpful discussions held with Walter Woodbury and Hans Hecht, and with A R Koch

References

1 PARLIN R B & H EYRING 1954 Membrane permeability and electrical potential *In* Ion Transport Across Membranes H T Clarke Ed 103–118 Academic Press New York N Y
2 ZWOLINSKI B J H EYRING & C REESE 1949 J Phys & Colloid Chem 53 1426
3 EYRING H R LUMRY & J W WOODBURY 1949 Record Chem Progress Kresge Hooker Sci Lib 10 100
4 JOHNSON F H H EYRING & M J POLISSAR 1954 The Kinetic Basis of Molecular Biology Wiley New York N Y
5 KATO H P B J ZWOLINSKI & J EYRING 1956 J Phys Chem 60 404
6 EYRING H & T F DOUGHERTY 1955 Am Scientist 43 457
7 FULTON J F 1949 Textbook of Physiology 619 W B Saunders Philadelphia Pa

EFFECTS OF SODIUM AND POTASSIUM ON REPOLARIZATION IN FROG VENTRICULAR FIBERS*

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Recently Hodgkin and Huxley (1952) defined the roles of sodium and potassium ions in the electrical activity of the squid giant axon These findings have prompted us to investigate the part these ions play in other tissues We present here a summary of our experiments on the way changes in the ionic composition of the perfusate affect the size and shape of the action potential of the frog ventricle Weidmann (1955) and Draper and Weidmann (1951) have shown that in Purkinje fibers the properties of membrane conductance changes are similar to those in the squid giant axon and that the phase of depolarization is probably produced by a large increase in this conductance However the repolarization phase of myocardial action potentials takes 500 to 1000 times longer than that of nerve and skeletal muscle Changes in the external concentrations of sodium and potassium ions are known to alter markedly the duration of the ventricular action potential This ion dependence suggests that with appropriate modifications the nerve sodium potassium hypothesis is applicable to cardiac muscle

The total ionic current through the fiber membrane can be estimated if it is assumed that the electrical circuit equivalent to the cell membrane is a resistance and a capacitance in parallel When the entire cell is excited simultaneously the longitudinal current and total membrane current are zero so the net membrane ionic current (I) must equal the negative of the membrane capacitive current The capacitive current is CdV/dt where C is the membrane capacity and dV/dt is the time derivative (slope) of the membrane action potential (V) Thus $I = -CdV/dt$ In these investigations V and dV/dt in single frog ventricular fibers were simultaneously recorded The change in membrane voltage and current effected by changes in Na and K concentrations give some information concerning the roles of these ions in ventricular repolarization

Methods

A frog ventricle was excised and perfused both inside and outside with a Ringer s solution whose Na and K concentrations could be altered Intracellular potentials were recorded with a Ling Gerard ultramicroelectrode flexibly mounted on a fine tungsten wire (Woodbury and Brady 1956) The time derivative of the membrane action potential was obtained by electrical differentiation (time constant of 1 or 5 msec) and was recorded simultaneously with the action potential on a dual beam oscilloscope The temperature was

This investigation was supported in part by Research Grants B462 and B823 from the National Institute of Neurological Diseases and Blindness of the National Institutes of Health Public Health Service Department of Health Education and Welfare Bethesda Md and by the State of Washington Fund for Research in Biology and Medicine Seattle Wash

maintained at 17 to 19° C The ventricle was excited by passing a 20-mAmp 2 msec, rectangular pulse radially outward through the ventricular wall In low Na solutions the response was delayed sometimes as much as 50 msec but no extracellular current that coincided with the repolarization phase could be recorded Therefore it was valid to use dV/dt as a measure of membrane ionic current

Results

The superimposed records in FIGURE 1 show the effects of changes in the extracellular Na concentration on the action potential (*AP*) The time base applies to each record but the voltage calibration in some of the records is slightly incorrect The stimulus artifact in 20 per cent Na was visible approximately 40 msec before depolarization The delay in response was much shorter in higher Na concentrations

At a constant stimulus rate of 20/min the duration (T_p) of the ventricular AP and external Na were linearly related The mean control T_p was 920 msec and the line had a slope of 10 msec/mM Na/l The ventricle rapidly became inexcitable in 15 per cent Na solutions This observation agrees with findings in other tissues (Purkinje tissue Draper and Weidmann 1951 myelinated nerve Huxley and Stampfli 1951 skeletal muscle Nastuk and Hodgkin 1950)

The action potential overshoot followed the Na concentration potential to about 60-per cent Na In lower extracellular Na concentrations the overshoot remained closer to zero potential than predicted from the Na concentration This behavior indicates a loss of intracellular Na in Na poor external media

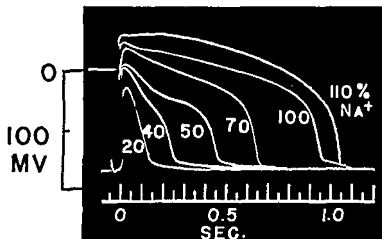


FIGURE 1 Superposition of action potentials recorded from a frog ventricle perfused with Ringer's solutions containing various concentrations of Na The zero potential and voltage calibration are shown at the left of the record

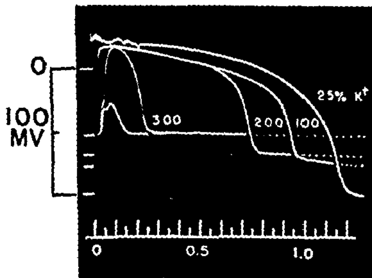


FIGURE 2 Superposition of action potentials recorded from a frog ventricle perfused with Ringer's solution containing various concentrations of K. The stimulus artifact and probable movement artifacts are visible at the beginning of repolarization in the 25 per cent K record

FIGURE 2 is a superposition of *AP*'s altered by changes in extracellular K while the Na was maintained at normal concentration. The two *AP*'s with the shortest duration were consecutive beats recorded in 300-per cent K shortly before the cell became completely inexcitable.

The T_p plotted as a function of external K is roughly hyperbolic and concave upward. Marked shortening of T_p occurred in high K and an elongation occurred in low K. The resting potential (*RP*) was not a simple function of the K concentration potential. In K free Ringer's solution the mean *RP* was 130 per cent of normal. The *RP* approached zero potential in concentrations above 32 times normal (80 mM/l). The overshoot of the action potential varied almost linearly with external K from 125 per cent of normal in 25 per cent K to 50 per cent of normal in 200-per cent K. With a reduced external Na and a variation of external K relations parallel to those in normal Na but at lower overshoot voltages were obtained.

The membrane ionic current proportional to $-dV/dt$ is shown in FIGURE 3 as a function of the extracellular Na and in FIGURE 4 as a function of K concentration. The first, second, and third phases of repolarization are measured by the first maximum rate of repolarization (not always present), the succeeding minimum rate (during the plateau), and the final maximum rate respectively (see the numbers on the derivative curve in FIGURE 3 inset). As the external Na concentration was reduced from normal the outward membrane current (defined as positive) in the first and second phases increased slowly until 60-per cent Na was reached (FIGURE 3). Below this concentration the

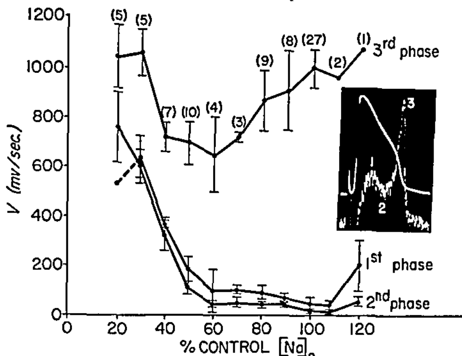


FIGURE 3 Extreme values (three phases of repolarization) of the membrane ionic current as a function of the external Na concentration The inset shows the action potential and its negative time derivative obtained in 40-per cent Na The three phases of repolarization are indicated by the numbers on the inset Noise is visible on the derivative record The number of records obtained in each solution is given in parentheses The vertical bars represent two standard errors of the mean

early outward current (first and second phases) increased sharply In contrast the late outward current (third phase) at first decreased with reduced Na and then increased parallel with the first and second phases In many cases the phases were indistinguishable when the solutions contained less than 40 per cent Na

Although the early outward current was little influenced by extracellular K the late current (third phase) was strikingly dependent on K (FIGURE 4 the 100 per cent Na line) This effect was markedly reduced by lowering Na to 70 per cent but the effect was larger again in 40 per cent Na There is limited information on solutions in which both Na and K were varied but a marked interaction between Na and K is clearly shown

Discussion

The object of this study was to investigate the ionic movements and conductance changes underlying the ventricular *AP* particularly those changes responsible for its extreme duration The available information is not sufficient to explain those changes definitively However these data combined with those in the literature do permit certain tentative conclusions and de

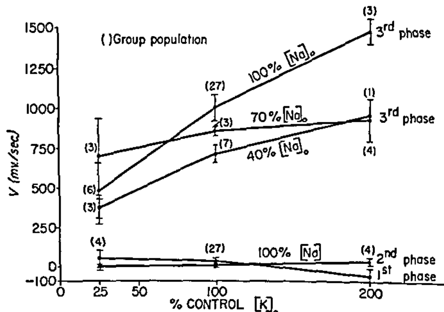


FIGURE 4 Extreme values of the time derivative of the action potential as a function of external K with the Na concentration held constant at various values

limitations that may be of interest A simple assumption is that changes in the concentration of an ion affect the *AP* only because the electrochemical gradient of that ion is changed, in other words because changes in ionic concentration do not alter membrane conductance The effects of Na alterations are generally explicable on this basis (FIGURES 1 and 3) A reduction in external Na reduces the inflow of Na ions consequently the amplitude and duration of the *AP* are reduced On the other hand changes in K produce large effects opposite to those that would be expected from the changes in the electrochemical gradient An increase in external K by increasing inward current supposedly would increase the duration of the *AP* Actually (FIGURE 2) high K shortens the *AP* markedly Similarly the slope of the third phase increases instead of decreases with K

Weidmann (1956) has measured total membrane conductance as a function of time during repolarization in Purkinje tissue Relative to early diastole the conductance during early repolarization (phase 1) is high but it falls rapidly to one third of the diastolic value during phase 2 and approaches the original conductance during phase 3 Assuming that this finding is applicable to the frog ventricle then the course of events during the *AP* may be somewhat as follows

Depolarization is probably the result of a sudden large increase in membrane Na conductance This increased conductance falls off rapidly in time but is still greater than resting membrane conductance for about 100 msec The potential is near V_N during this period (phase 1) Total membrane conduct

ance falls to about one third of the diastolic value after 100 msec. and since the potential is near zero (phase 2), Na conductance must be greater than K conductance and their sum during this period must be less than it is during rest. In other words, K conductance has fallen. This statement is based on the assumptions that only Na and K contribute appreciably to membrane conductance and that current flow results only from Na and K ions moving along their concentration gradients. This is the case for squid giant axon (Hodgkin and Huxley, 1952). During repolarization, however, the membrane currents are much smaller in the frog ventricle than in the squid axon, and it is conceivable that active ion transport plays an important role. During phase 2 the gradual potential fall merges into phase 3, where the rate of repolarization increases greatly. It might be expected that the fast rate of repolarization is a voltage dependent increase toward the resting value of K conductance. However, the dramatic increase in repolarization rate produced by increasing external K is difficult to explain. Keynes (1954) has shown that in frog sartorius muscle an increase in external K increases the Na efflux. If active Na efflux occurs as a charged moiety, then the increased rate of repolarization during phase 3 might be attributed to an increased outflux of Na. Thus the K effect could be explained in terms of a known phenomenon. This explanation is simple and understandably attractive, but the difficulty of constructing any mechanism that will behave in this manner remains. A more complete analysis must await further experimentation.

References

DRAPER, M. H. & S. WEIDMANN. 1951. Cardiac resting and action potentials recorded with an intracellular electrode. J. Physiol. **115**: 74-94.

HODGKIN, A. L. & A. F. HUXLEY. 1952. A quantitative description of membrane current and its application to conduction and excitation in nerve. J. Physiol. **117**: 500-544.

HUXLEY, A. F. & R. STAMPFLI. 1951. Effect of potassium and sodium on resting and action potentials of single myelinated nerve fibers. J. Physiol. **112**: 496-508.

KEYNES, R. D. 1954. The ionic fluxes in frog muscle. Proc. Roy. Soc. London. **B142**: 359-382.

NASTUK, W. L. & A. L. HODGKIN. 1950. The electrical activity of single muscle fibers. J. Cellular Comp. Physiol. **35**: 39-73.

WEIDMANN, S. 1955. The effect of the cardiac membrane potential on the rapid availability of the sodium carrying system. J. Physiol. **127**: 213-224.

WEIDMANN, S. 1956. Elektrophysiologie der Herzmuskelfaser. Huber. Bern, Switzerland.

WOODBURY, J. W. & A. J. BRADY. 1956. Intracellular recording from moving tissues with a flexibly mounted ultramicroelectrode. Science. **123**: 100-101.

THE PULSATILE NATURE OF THE RELEASE OF POTASSIUM FROM HEART MUSCLE DURING THE SYSTOLE*

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My colleagues James M O Brien and Irene Bay and I have produced direct evidence that the potassium release of cardiac contraction or activity is truly pulsatile A turtle heart is heavily labeled *in vivo* with intraperitoneal K^{42} The isotope must be prepared in the intense neutron flux of the Low Intensity Testing Reactor at Oak Ridge The excised heart is perfused (FIGURE 1) and the outflowing perfusate is caught on a filter paper strip moving past on a timed kymograph The strip is cut into rectangular samples that are serially collected at known times The electrocardiogram and a myogram are recorded simultaneously The potassium release of activity may thus be related in time to the electrical events A second radioactivity is added as a volume indicator in the perfusion fluid This may be I^{131} albumin or inorganic phosphate tagged with P^{32} and it is counted after the potassium K^{42} has been allowed to decay through its short half life An arithmetical division of the K^{42} count by the volume indicator count on each paper segment then gives us the concentration of potassium K^{42} for that particular sample

FIGURE 2 is a typical curve for one of the two hearts on which runs have been successful in the last four years The ECG waves are above and the concentration waves for K^{42} are below—our so called efflugram record The first K^{42} wave is for a systole elicited by electrical stimulation at the A V junction and the second wave is for an idioventricular beat Thus we see that the wave of release is real and not the result of electrolysis due to the stimulating current Note that there are about seven samples represented in the upstroke of the wave and about forty in the entire wave The samples measured may each contain as little as 0 003 ml of perfusate There is no correction for travel time on this chart

Note that the perfusion irrigation is not by way of the ventricular cavity but only by way of the coronary vessels (FIGURE 3) Cannulation for the inflow is into the single coronary artery Occasionally two coronary arteries arise independently from the innominate artery and thus spoil an experiment in which we have invested more than a hundred dollars worth of isotopes Unfortunately the outflowing venous coronary vessels do not collect into a single vessel for cannulation but open by several vents into the neighborhood of the sinus venosus The collective outflow from these veins is allowed to flow down the outside of a solid glass stylus penlike in form The stylus is anchored by a ligature about the A V junction The trimmed right auricle and the sinus venosus drape about this stylus like the cloth of an umbrella Resting flow is very steady (lower curve of FIGURE 5)

* This study was supported by the United States Atomic Energy Commission (Contract No AT(40-1)1301) Washington D C the Life Insurance Medical Research Fund (G55 28) New York N Y and the American Heart Association New York N Y

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FIGURE 4 shows the general layout of the apparatus

FIGURE 5 shows our most successful run in a serial recording of six systoles The gradual fall in base line whatever its cause is real It is not due to the attenuation of the tagging within the heart

The outflowing K^{42} naturally suffers a travel time and a scatter phenomenon as it travels from each capillary, a variable distance, to the tip of the stylus

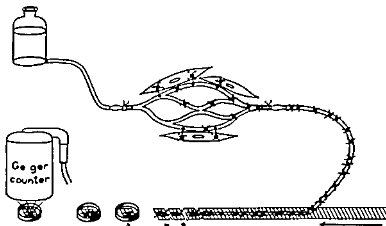


FIGURE 1 Principle of effluography

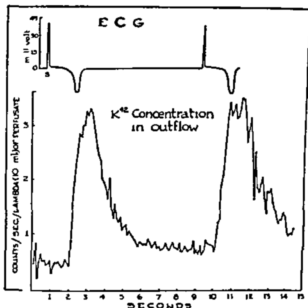


FIGURE 2 The effluogram

FIGURE 6 shows how we have attempted to calibrate for this It is a model of the coronary circulation made with strings Each string travels the full length of the coronary bed artery to vein, but traverses only one capillary loop In the upper figure the arches represent capillary loops Thus, the strings enter the loops from the artery on the left and leave the loops to travel

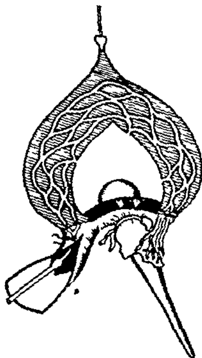


FIGURE 3 Coronary cannula and stylus.

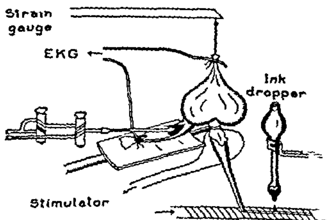


FIGURE 4 Heart mounted over kymograph

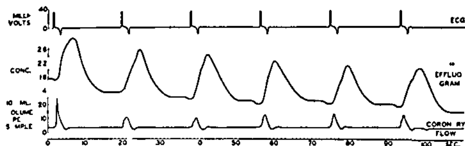


FIGURE 5 Effluograms Six consecutive systoles electrically stimulated The lower recording is of volume collected per sample or per 0 096 second

to the vein on the right On each end of the model the strings are tied tightly together so that they may be slipped collectively back and forth through the model to represent flow The scatter of K^{4} is illustrated by staining the strings at the peak of each arch or capillary loop Then as the strings are drawn collectively to the right these stained segments take on the pattern illustrated at the right

A graphical representation of this scatter is shown above at the right It is plotted by imagining the vein or bundle of strings to be cut into egments *The number of stained elements in each segment is then plotted vertically to* construct the plot shown above Note that this is analogous to plotting concentration in the outflow against accumulated volume

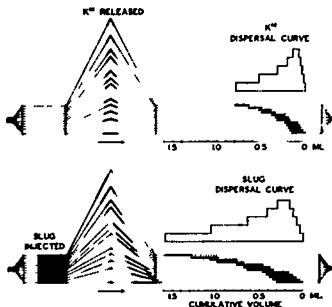


FIGURE 6 String model of the mechanism of vascular dispersal The upper curve represents the dispersal of K^{42} released into capillaries The lower curve represents the dispersal of the injected slug

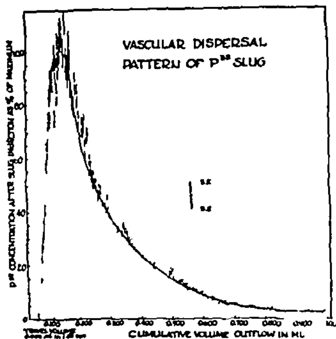


FIGURE 7 Actual slug dispersal curve

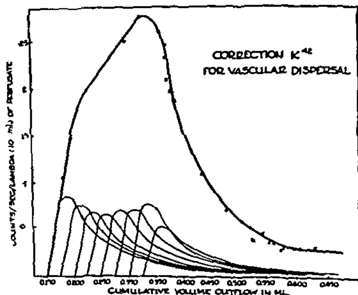


FIGURE 8 Volume effluogram (above) showing the graphical summation of pattern release curves (below)

It might be thought that changes in flow would distort the shape of this scatter pattern If the strings are jerked back and forth to mimic variable flow rate however it will be seen that this pattern is retained In actual plotting this pattern will be obtained only if concentration is plotted against accumulated volume If instead the concentration is plotted against serial *time flow changes will indeed distort the pattern We have thus resorted to* the stratagem of plotting all concentrations against accumulated volume and have thus caught this uniformity of pattern

Since it is impossible to construct this ideal scatter pattern we mimic it by constructing the pattern for a parcel of a third radioactivity injected suddenly into the coronary artery This will produce the pattern modeled in the lower diagram in FIGURE 6 Note that since the travel distances are roughly double this pattern will be twice as wide as the ideal pattern for the release of potassium mid length of each capillary loop

Such a pattern is shown in FIGURE 7 as constructed from the pattern set by an actual parcel after injection into the coronary artery This injection is accomplished by catching a third indicator radioactivity in the plug of a stop cock (left side of FIGURE 4) A sudden turn of the stopcock at the end of a series of regular runs then allows us to construct the pattern curve as shown in FIGURE 7

In FIGURE 8 we imagine what series of pattern curves representing successive releases in time of K^{42} into each of the capillaries would when added give the over all curve that is drawn through actual experimental points This is accomplished by a graphical differentiation in which one pattern curve is subtracted from the over all curve a second pattern curve is substracted from the residue of points and so on until all the area of the ove all curve has been used up Thus in FIGURE 8 the total area of the over all curve is the sum of the areas of all the individual pattern curves shown below

Since this is a plot of concentration vertically against accumulated volume horizontally the area of each of these pattern curves represents a mass of released K^{42} The area of each pattern curve is compressed into a rectangle the width of which is equal to the accumulated volume between two successive upswings of pattern curves Later this same area is compressed into a time

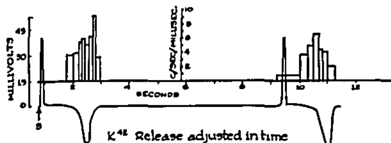


FIGURE 9 Chemocardiogram The rectangles are K^{42} release parcels extrapolated backward in time for vascular travel and dispersal The altitudes of each rectangle are the rate of release for the interval

interval covered by this same collection period and is fitted against the corresponding electrocardiogram as shown in FIGURE 9

In summary our firm conclusion is that the release of potassium is indeed pulsatile A less firm impression is that the release begins during what Weidmann calls the ' plateau and continues with special rapidity during the [illegible] phase of the repolarization wave as recorded with intracellular electrodes

NORMAL AND ABNORMAL TRANSMEMBRANE POTENTIALS OF THE SPONTANEOUSLY BEATING HEART*

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The outline of the mechanisms by which the heart initiates its ceaseless repetitive contractions begins to emerge from the careful deductions of the series of experiments discussed in the preceding presentations For some time this laboratory has recorded and analyzed transmembrane potentials of single cardiac fibers of the spontaneously beating heart usually *in situ* and with the circulation intact We hoped thereby to obtain further information on the nature of the surface phenomena that are of interest to the clinical investigator confronted with the complexities of an electrocardiographic curve I have chosen a pedestrian course of presentation that will impress some as superfluous but that may be of aid to others in assessing the difficulties of the road over which the previous writers have traveled so easily

In the following pages some aspects of transmembrane potentials will be discussed as they appear of particular interest to those concerned with the electrical phenomena of the beating heart as a whole In many aspects the information is as yet incomplete but a dim outline of the completed structure appears on the horizon I have omitted a detailed description of the normal components of cardiac transmembrane potential these may be found in recent reviews [1,2]

Technical Aspects

Not all monophasic records obtained by a microelectrode are from intracellular positions and not all microelectrodes yield similar results The decision of what constitutes a transmembrane potential and what may be a demarcation or injury effect is difficult Both yield monophasic or semimonophasic curves that are closely related but one kind cannot always be substituted for the other (see below) Since direct observation of the electrode position as illustrated in FIGURE 1 is not possible during the actual experiment certain criteria must be satisfied before a record may be labeled as likely to represent transmembrane potentials This requires a qualitative analysis of many parameters on a descriptive basis that goes beyond mere measurements of height and duration TABLE 1 lists a type of record analysis that has been found useful The equipment usually built for the purpose must be thoroughly understood and it is essential that the recording glass capillary be tested before insertion It must have the desired taper which may vary for different tissues to be examined and the internal diameter of its tip must be 1 μ or less [3] Beyond a certain critical tip diameter the recorded potentials decrease sharply presumably due to membrane leakage (FIGURE 2) It is

This study was supported in part by grants from the Utah Heart Association the National Heart Institute of the National Institutes of Health Public Health Service Department of Health Education and Welfare Bethesda Md and CIBA Pharmaceutical Products Inc Summit N J

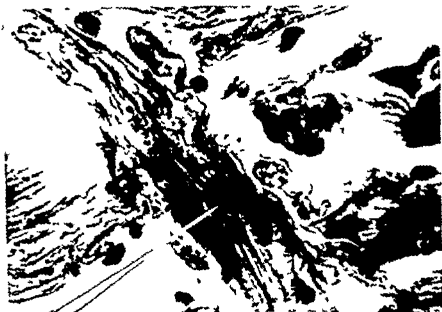


FIGURE 1. Microelectrode and myocardial fiber (frog ventricle). The tip of the microelectrode measure 1.0.6 μ. Superimposed photographs; hematoxylin and eosin stain.

necessary and obvious from FIGURE 2 that frequent checks be made during an experiment either by direct microscopic inspection of the needle or by impedance measurements of the recording system in order to ensure that the tip of the electrode has remained intact. The use of a floating tungsten wire glass capillary electrode[4] has facilitated recording from moving tissues *in situ* and has all but eliminated earlier devices that were necessary to safeguard the electrode.[2] The placement of the indifferent electrode, the characteristics of the recording apparatus itself, and the occurrence of junction potentials at the cell electrode boundary are some of the additional factors that may influence the final record and need to be evaluated.[1]

TABLE 1

DATA ANALYSIS: INTRACELLULAR RECORDS

Characteristic of intracellular record: (A) size in mv and (B) unbroken depolarization

Resting potential	Size in mv
	Prepotentials
	Afterpotentials
Action potential	Size in mv
	Overshoot
Action potential duration	Length in sec
Excitation	Rate of depolarization mv/sec
	Duration of depolarization msec
Recovery	Phases of repolarization
	Rate of repolarization mv/sec (for each phase)

Corrected for standard action potential

Once the needle has penetrated the cell and the membrane has sealed itself around it long repetitive records may be obtained even from the spontaneously beating heart *in situ* FIGURE 3 represents the typical experimental sequence of a cellular run insertion followed by several cycles demonstrating resting

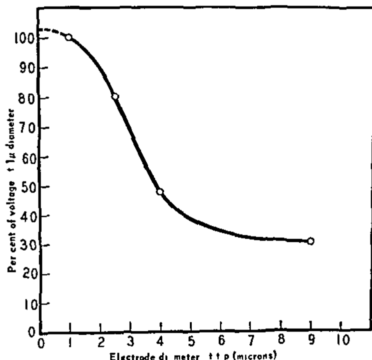


FIGURE 2 Observed transmembrane potential as a function of the external diameter of the recording electrode (Woodbury *et al* [8])

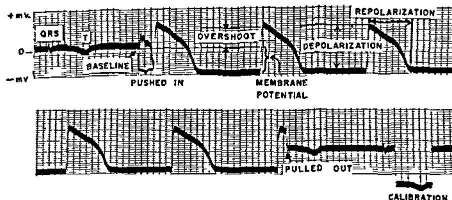


FIGURE 3 Sequence of cellular events during cardiac excitation (frog ventricular fiber *in situ*) membrane potential plus overshoot equals action potential Note the steady dia stolic resting potential and the slow recovery process Calibration 50 mv time lines 0 1 ec

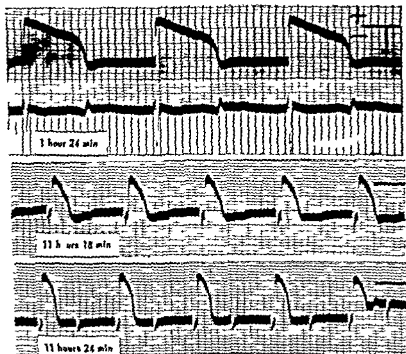


FIGURE 4 Transmembrane potentials (frog ventricular fiber *in situ*) The upper record shows the cellular potentials recorded together with the surface electrogram of a closely adjacent region 1 ½ hr after the beginning of the experiment Note the positive afterpotentials The middle record shows the same preparation after 11 hr of uninterrupted spontaneous activity Four minutes before the recording the heart ceased to beat but it continued to respond to electrical stimulation (see stimulus artefact) The resting action potential has changed little in magnitude but the action potential duration has been shortened and the rate of recovery has been altered Strong prolonged afterpotentials are present. In the lower record made 5 min. later the heart has responded to alternate stimuli at higher rates Further shortening of the action-potential duration has occurred without affecting the resting potential or overshoot Calibration (upper right corner) 50 mv horizontal bar zero line time lines 0 1 sec.

potential membrane depolarization polarization reversal and overshoot and recovery and afterpotential With the recording device still running the needle is then withdrawn and a calibration is added (50 mv) FIGURE 4 demonstrates that a physiologically active preparation may still be observed many hours after the beginning of an experiment although the shape of the recovery may have changed significantly when compared to the control It is possible to obtain two simultaneous intracellular records by placing microelectrodes into different fibers even under a variety of physiological states (FIGURE 5) The *in situ* preparation does not lend itself however to the insertion of two electrodes into the same fiber and experiments with clamped potentials as reported by Weidmann[3] presumably cannot be carried out in such preparations

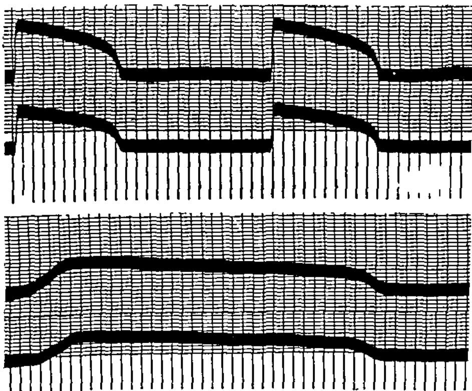


FIGURE 5 Simultaneous intracellular records using 2 microelectrode recording systems The upper records are at 16 C the lower records at 2 C

Magnitude of Cellular Resting and Action Potentials

The order of magnitude of the recorded potentials and the remarkable constancy from species to species never ceases to astound those accustomed to the small sizes and great variabilities of the surface electrocardiograms (FIGURE 6) although it has been obvious since Bernstein s estimates[5] that transmembrane potentials should measure between 60 and 80 mv Bernstein postulated that the potentials should be related to the logarithm of the concentration ratios of extracellular and intracellular ions and suggested potassium as the crucial cation involved He was one of the first to suggest the use of equations describing diffusion potentials for liquid junction boundaries of solutions containing different concentrations of the same electrolyte Boyle and Conway[6] have restated the problem for biologic tissues and have suggested that the resting potential is related to differences in concentration of extracellular and intracellular K^+ and Cl^- distributed according to the Donnan equilibrium If this is accepted as a general principle even if arguments may be brought against it[7] then constant values may be expected irrespective of tissue and species On the other hand surface records are dependent on heart size Re

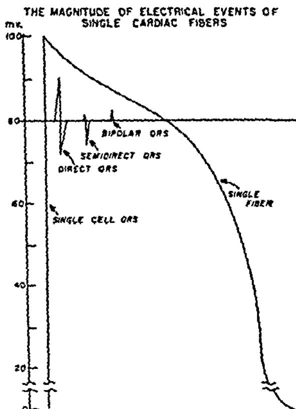


FIGURE 6 Diagrammatic repr sentation of the magnitude of transmembrane potentials as compared to surface electrocardiograms As an example the frog ventricular fiber shows voltages from 50 to 100 times higher than those observed in recording the human electro cardiogram Surface records are related to membrane current density and to the rate of voltag changes and are a function of the total myocardial mass They are independent of action potential magnitudes

cent measurements of the magnitude of the surface dipole moment of the intact hearts have confirmed the relation of action currents (and by inference of action potentials) to the total myocardial mass[5]

Variations in magnitude of cellular potentials have been reported by dif ferent observers and for various species or types of myocardial fibers These differences are not striking and Weidmann[1] suggested that they may depend on myocardial fiber size Naturally it is more difficult to obtain satisfactory records from smaller fibers than from larger ones although it seems that with improvement in technical skill voltages may be raised TABLE 2 lists measure ments from various tissues and species recorded at various times but in the same laboratory The last series of measurements on frog ventricular fibers gave values comparable to those reported for the squid giant axon or for the Purkinje ti sue of the dog or the goat The influence of nutrition seasonal

TABLE 2
MEMBRANE RESTING (MP) AND ACTION POTENTIAL (AP) OF CARDIAC MUSCLE FIBER (MV)

	No	MP	AP
Chick embryo	195	39 3 (0 7)	53 5 (1 4)
Turtle sinus isolated	39	36 1 (0 8)	42 0 (0 9)
Frog *in situ* series A	60	64 5 (2 3)	77 2 (2 9)
Frog *in situ* series B	73	80 2 (1 9)	95 3 (2 2)

Mean and S E

changes or other metabolic factors should also be considered since some groups of animals seem to yield lower values than others

Neither action nor resting potentials are greatly influenced by changes in temperature[1, 3, 9, 11] or in heart rate[3, 12] unless the rate rises to excessive levels Thus during the extremely fast rates of a heart in ventricular fibrillation, the height of the action potential decreases sharply without significant changes in membrane resting potentials (FIGURE 7) At the height of the response (at rates from 200 to 800/min) the cell does not completely depolarize and restoration of the resting potential commences when the inside is still negative to the outside of the cell or before polarization reversal has occurred (undershoot)[13]

The relation of resting potential action potential and overshoot in cardiac

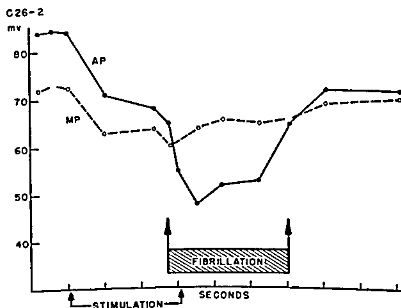


FIGURE 7 Membrane resting and action potential of ventricular fibers during ventricular fibrillation (bullfrog *in situ*) The rapidly fibrillating ventricle causes excitatory responses of low amplitude in the face of an unchanged resting potential (Hecht and Brady unpublished) AP membrane action potential MP membrane resting potential

TABLE 3
SAMPLE ANALYSIS OF INTRACELLULAR RECORDS (FROG *in situ*)

	T min	t °C	Cy l sec	MP mv	AP mv	AP_d sec	D_g mv/sec	D msec	R_s1 mv/sec	R_s2 mv/sec	R_s3 mv/sec
Normal		25	0.44	67.5	80.2	0.62	3530	22	155	48.6	1175
KCl	0	22	0.83	100.0	132.5	0.55	2230	22	258	93	662
	0		0.72	91.7	104.0	0.55	3920	25	138	99	741
	3.6		0.82	**27.8**	**61.1**	0.45	5250	27	**334**	**187**	**264**
	6.6		0.72	**28.9**	**58.9**	0.43	4700	22	89	73	**654**
	24.0	20	0.86	85.5	99.0	0.59	5340	22	126	85	800
CaCl	0	24	1.19	69.8	97.9	0.53	4820	14	152	97	650
	6.2		1.30	58.7	91.4	0.55	4100	18	**438**	77	446
†	16.6		1.31	67.2	98.9	0.64	4670	18	193	90	530
BaCl	0	19	0.47	92.1	107.0	0.69	3500	67	158	90	383
	2.2		0.48	**55.4**	**65.8**	**1.25**	3380	67	195	62	**148**
	20.6		0.39	70.6	96.3	**1.24**	2310	67	155	58	**114**

* Corrected for action potential = 100 mv
† After washing
Bold type denotes statistically significant values ($p < 0.05$) *T* time *t* temperature *MP* membrane resting potential *AP* membrane action potential AP_d action potential duration D_g slope of depolarization *D* duration of depolarization and R_s1–R_s3 slope of repolarization phases 1 2 and 3

muscle has been discussed in previous papers giving additional support to the concept that for heart muscle (as for nerve) the presence of a transmembrane potential is dependent to a large measure on sodium and potassium conductance with the exchange of minute amounts of these ions across the membrane [1, 2, 11, 14] The *in situ* preparation does not lend itself easily to rapid changes of extra cellular electrolyte concentrations and little can be added to what has been said before (pp 665) However topical application of concentrated electrolyte solutions (TABLE 3 FIGURES 20 and 22) and records from the isolated spontaneously beating perfused heart have in general confirmed a certain dependence of the magnitude of the cellular potentials on the ratio of external to internal electrolyte concentration Thus external increase in K^+ sharply reduced the magnitude of the resting potential (TABLE 3 FIGURE 22) while perfusing an isolated frog heart preparation with a K^+ free tyrode solution increased the resting potential but not to the expected degree [17] In papillary muscle these effects may be antagonized by changes of Ca^{++} in the same direction [2] In the atrial tissue of cats and frogs vagal stimulation or the application of acetylcholine causes an increase in the resting potential that may or may not be associated with changes in the repolarization process [2] This effect was absent in recent studies using atria of rats [19]

Duration of Action Potential

Cardiac muscle differs from nerve and skeletal muscle by its exceptionally slow return to the resting state that is almost exclusively the consequence of a

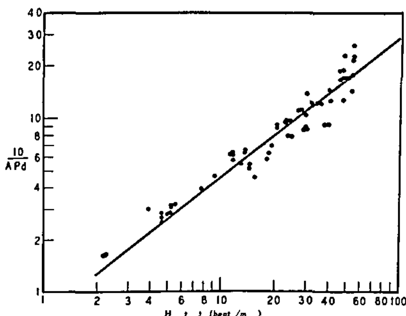


FIGURE 8. Reciprocal relation of action potential duration as a function of the heart rate, log log scale (Woodbury *et al.*[8])

marked prolongation of the repolarization process. In a normal myocardial fiber the duration of the action potential is dependent on (1) the heart rate and (2) the temperature.[1,3,9,12,19,21] Since these factors are interdependent, appropriate corrections must be made if action potentials are to be related to only one or the other. FIGURE 8 shows a log/log plot of heart rate versus the reciprocal of the duration of membrane action potentials with the temperature dependence eliminated algebraically.[8] The slope of the line is the ratio of the temperature coefficient for the action potential duration and for the heart rate, and it has a value of 0.8. In other words, as the heart rate increases, the action potential duration decreases in proportion to the 0.8th power of the rate. This logarithmic relationship holds only for frog muscle, but it is of interest since a similar dependence has been demonstrated for the QT interval to the heart rate in surface leads of man.

The duration of the excitatory state is a sensitive indicator of myocardial integrity. It may normally vary from fiber to fiber.[8,20] Modern electrocardiographic theory requires that such differences should exist, perhaps between subendocardial and subepicardial layers (pp. 937). Beyond the fact that intraventricular differences in the duration of the action potential can occur, confirmation of this concept is still lacking.

Striking differences in the duration (and form) of the action potential between ventricular and atrial musculature have been observed under various experimental conditions.[1,19,21] It is tempting to assume that this is related to excess accumulation of acetylcholine and vagal innervation, except that these

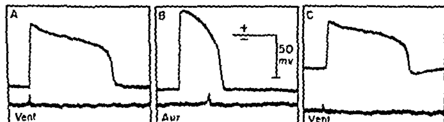


FIGURE 9 Frog heart *in situ* (pithed) Figures A and C show the ventricular action potential B shows the atrial action potential obtained shortly after A and before C Note the shortening of the action potential duration in B and the loss of phase 1 of recovery A ventricular surface lead is recorded simultaneously (retraced photograph of scope screen)

differences may be observed in denervated animals and excised preparations or may be in evidence before innervation has occurred FIGURE 9 shows differences in action potential duration between the atria and ventricle of the myocardium of a pithed frog and FIGURE 10 illustrates an obvious decrease in atrial action potential duration in the chick embryo commencing at the fourth day and before extrinsic innervation has been established [9] This suggests that the differences in some way depend on the maturation process of the myocardium In a well functioning excised turtle heart such differences were not present (FIGURE 11) It should be noted that some of the shortening reported may be the result of tissue damage influencing the thin atrial muscle sheets to a greater extent than the robust working myocardium

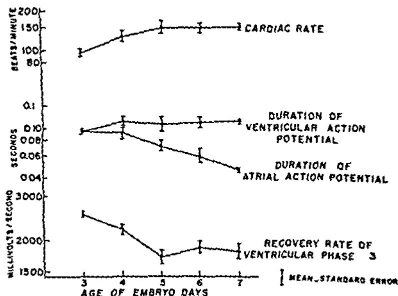


FIGURE 10 Increase in cardiac rate and decrease in duration of atrial action potential in the growing chick embryo The records were obtained with the circulation intact The changes occur before extrinsic innervation is established (Fingl *et al*)

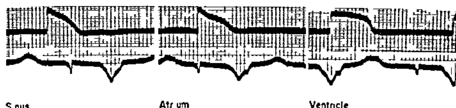


FIGURE 11. Membrane resting and action potential of the spontaneously beating excised turtle heart. There is no consistent difference in the shape of records obtained from the sinus, atria, or ventricle and there is no difference in action potential duration. Simultaneously recorded surface records show excitation of the sinus region, the atria, and the ventricles. Note the remote effects of ventricular depolarization in records obtained from the sinus region and the atrium, presumably caused by changes occurring under the "indifferent" electrode. Time lines 0.1 sec. (Brady and Hecht[28])

FIGURE 12. Frog ventricular muscle *in situ*, high speed records of depolarization. Note the smooth S-shaped configuration without discernible phase differences. Record *D* was obtained after topical application of quinidine. *E* shows the same preparation after recovery. The surface potentials are recorded in *A* and *B*.

Changes in duration of action potentials are usually the result of changes in the various processes of repolarization and will be considered in that connection It should be pointed out that shortening of the action potential duration in some instances shows a strong correlation with the magnitude of the depolarization overshoot ($p < 0.02$ in the ventricular myocardium of the frog following administration of digitalis glycosides[17] and similar observation on rat atria with acetylcholine and carbachol[18])

Polarization Reversal (Depolarization)

Membrane depolarization and reversal of polarization (overshoot) is rapid and smooth (FIGURE 12)[1, 9] A record that displays notches or breaks in the rising limb of a transmembrane change represents injury potentials rather than true membrane effects orderly rapid depolarization is one of the few absolute characteristics of intracellular records The S shaped slope of the curve reaches a value that in nerve closely approximates the sodium potential (a potential difference that should exist if only sodium were moving across the membrane) In cardiac fibers it is often less pronounced but here as well as in nerve it coincides with a sharp fall in membrane resistance[1, 2] It has been assumed that the process represents Na influx across a fundamentally altered membrane[1, 2, 14, 16] The rate of this process is temperature-dependent (FIGURE 13)[1, 2, 3, 10, 11, 9] For frog ventricular fiber at room temperature depolarization time (measured from 10 to 90 per cent of the total deflection) ranges from 10 to 20 msec falling off logarithmically with rising temperatures ($\log$ of $Dt = 1.6 - 0.03\,t$) FIGURE 13 demonstrates that at a temperature of 40° C a frog ventricular muscle (if not damaged by temperature) would be expected to depolarize in 2 to 3 msec a figure that corresponds with those reported for mammalian ventricular fibers[10] There are no striking changes in rise time between atrial and ventricular fibers but the thick rapidly conducting Purkinje cells that show somewhat larger membrane resting potentials depolarize during less than 0.5 msec[1] No information is available concerning slowly conducting tissues such as the atrioventricular node In addition to the temperature effect which is of little practical consequence the speed of polarization depends on the initial starting level of the membrane resting potential the higher the resting potential the steeper the rise[1] Therefore procedures and agents that affect primarily the resting potential have an indirect effect on the depolarization time The values of FIGURE 13 are based on an average resting potential of 70 mv

Except by these factors the time and rate (slope) of this process are not easily influenced There are compounds that stabilize the membrane and lock polarization This results in a preparation that does not conduct an impulse[1] but that remains excitable by virtue of a maintained resting potential These blocking agents are the surface anesthetics certain antihistaminics and quinidine and quinidinelike substances[22] In cardiac muscle procaine procaine amide and quinidine have long been used to block or to retard impulses and their action may now be interpreted in terms of their influence on the depolarization process TABLES 4 and 5 show the effects observed with quinidine gluconate (Eli Lilly & Company Indianapolis Ind) and with procaine amide

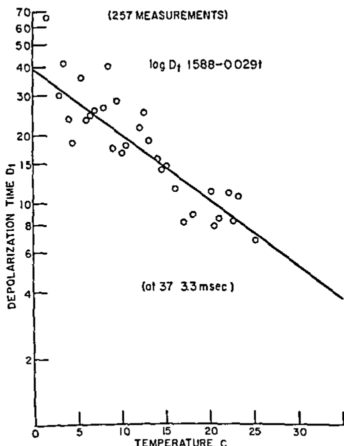


FIGURE 13 Temperature dependence of depolarization time (least square method) Frog ventricular fiber *in situ*

FIGURE 12D and 21 illustrate typical records When carried further polarization may be locked causing the heart to cease to beat but to remain essentially excitable (FIGURE 14) This action is accomplished without change in membrane resting potential, or in membrane resistance and it has been considered as blocking sodium transport across the fiber

The onset of cellular depolarization is fairly abrupt It begins with a slight

TABLE 4

DEPOLARIZATION TIME (MSEC) FOLLOWING TOPICAL APPLICATION OF QUINIDINE GLUCONATE (FROG *IN SITU*)

	Control	Vehicle	Quinidine
DB 22	10 (1 41)		28 5 (0 07)
DB 23	9 (0 08)	7 (0 09)	20 6 (3 8?)
DB 30	9 (0 06)	10 (0 23)	22 3 (6 80)

Mean and S E

TABLE 5
SAMPLE ANALYSIS OF INTRACELLULAR RECORDS (FROG IN SITU)

	T m	t C	Cycl sec.	MP m	AP m	APd sec	Dg m √sec	Dt msec	Rs1 m/sec	R4 m √sec	Rs3 m √sec
Normal		24	0 61	80 8	98 5	0 59	4200	16	—	128	2100
Digitalis	0	25	0 93	74 0	104 0	0 63	3200	36	134	68	2420
	8		**1 02**	59 3	**34 1**	**0 18**	**9100**		3600		
	18		**2 46**	62 3	**34 1**	0 09	9300		2930		
Acetylcholine	0	25	1 41	64 2	75 8	0 65	18 00	22	84	57	754
	1		**5 40**	**24 7**	**25 0**	**0 43**	6600	22	54	26	**189**
	10		2 46	53 5	67 1	0 56	17250	22			583
Procaine HCl	0	12	2 61	86 8	112 5	1 29	3380	29	19	49	493
	27	11	3 62	62 3	126 7	1 46	**1220**	**61**	37	59	**217**
	43	14	**5 06**	76 0	110 0	1 56	**1220**	**67** (140)		64	349
Quinidine Gluconate	0	22	0 67	75 0	100 0	0 88	3890	32	161	39	3900
			0 65	81 6	108 2	**1 18**	**1940**	**90**	93	38	**1265**
			0 70	80 6	89 1	**1 20**	**2940**	**68**	69	88	**2120**

Corrected for action potential = 100 mv
Bold type denotes statistically significant values ($p < 0.05$) The symbols are the same as those used in TABLE 3

decrease in membrane potential followed by a rapidly increasing decrement (FIGURE 15) When a critical value has been reached the cell will reverse polarization rapidly This threshold potential determines cardiac excitability and using Hodgkin's concept may be defined as the value at which sodium inward current exceeds potassium outward flux It has been suggested that the depressing effect on heart rate and on excitability known for Ca^{++} vagal stimulation and acetylcholine[21, 3, 25] may be related to their influence on the threshold potential of pacemaker areas In cardiac fibers the membrane holds a stable value until late in presystole when depolarization is initiated from surrounding areas (FIGURE 15) This is not true for cell groups located within the sinus region of the right atrium the spontaneous pacemaker region of the heart[1, 10, 11, 0, 4, 5, 6, 60] Here a leaky membrane causes a gradual and continuous loss of membrane potential either throughout the diastolic period or in presystole (FIGURE 16) a state of affairs that can be accentuated by NaCN or 2 4-dinitrophenol[1] The causes for this localized diastolic depolarization are not known but the fact that such a cell would act as a pacemaker by spontaneously reaching the threshold potential is readily understandable It seems obvious that such behavior cannot be confined to this region alone but that it is a potential characteristic of cardiac fibers Under certain circumstances other fiber groups may act in a similar manner, controlling the heart from an ectopic pacemaker focus

Repolarization

The return of the cardiac cell to the resting state is a prolonged process when compared to nerve and skeletal muscle It commences fairly rapidly flattens

FIGURE 14. Locked polarization and membrane stabilization following topical application of a pellet soaked with 1 per cent quinidin gluconate. A portion of the last spontaneous beat is seen followed by cellular arrest for 1 min 19 sec (continuous recording). A spontaneous beat of 68 mv complete with overshoot occurs at the end of the period (mechanical artefact is seen in the plateau). At the end of the record the needle is withdrawn demonstrating the isoelectric level.

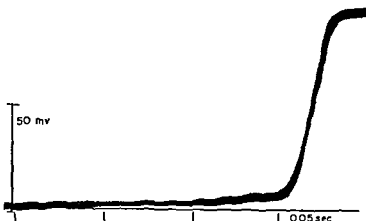


FIGURE 15. Frog ventricular fiber depolarization recorded at high speed. Note the gradual and minimal decrease in the resting membrane potential just prior to excitation. This is rarely discernible in low speed records.



FIGURE 16. Sinus potentials of spontaneously beating excised turtle heart. Note the steady loss of resting potentials and the presystolic prepotentials (lower right record)—two characteristic responses of pacemaker regions. The shape of the action potentials is considered abnormal (unphysiological preparation). Brady and Hecht.[29]

out to a plateau of long duration and finally gathers speed again as it approaches the diastolic resting level. Thus there are at least three phases clearly recognizable in all normal records from ventricular musculature (FIGURE 17). These phases display different rates of recovery (slopes) and entirely different temperature coefficients and respond differently to abnormal conditions (FIGURE 18).[8] One may assume that different metabolic processes are involved with each step. This series of rate processes appears in striking contrast to the smooth and rapid course of depolarization. Beyond this very little is known but by analogy it has been tempting to correlate events with ionic currents following Hodgkin's concept of nerve excitation (see below).

FIGURE 17. Membrane action potential of frog ventricular fiber *in situ*. The slope (m./sec.) and duration (sec.) of the three phases of recovery are indicated. Time lines 0.1 sec.

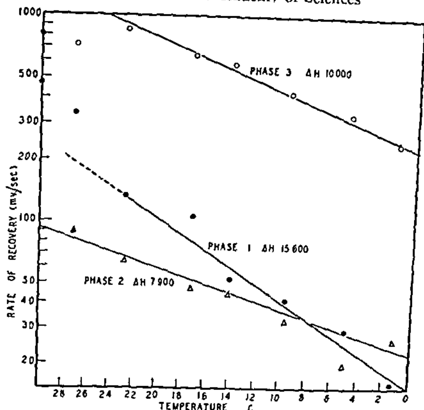


FIGURE 18 Rate of recovery of the three phases of repolarization as a function of temperature (*Arrhenius plot for monomolecular reactions*) ΔH is heat of activation in cal/M/degree (Woodbury *et al* [3])

Differences seem to exist between different types of tissues examined a much more rapid fall in repolarization phases has been reported for atrial tissue than for ventricular myocardium[1, 9, 19, 1] and for Purkinje fibers the dominance of phase 1 seems characteristic[1, 19] These effects are not absolute and one pattern may merge into the other The processes of repolarization are easily altered and constitute a sensitive indicator of myocardial function *A common response presumably unspecific is the transformation of the* multiphasic curve of long duration into a short single spike reminiscent, except for timing of the configuration of cellular potentials of skeletal muscle or nerve (FIGURE 19) In the case of digitalis administration as well as during infusion with low potassium fluids this response (or spike formation) is preceded by a period of lengthening of the action potential duration[17, 22] The spike formation is the result of an ever increasing rate (steeper slope) of phase 1, with phase 2 at first little affected and phase 3 increasing in length and decreasing in slope This may represent an end stage prior to irreversible membrane damage Eventually phases 2 and 3 disappear entirely[3]

Changes in repolarization necessarily result in changes in duration of the

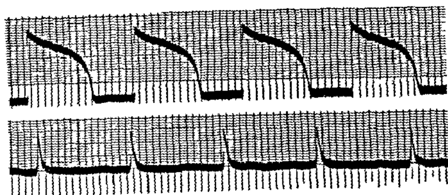


FIGURE 19 Configuration of action potential at the height of the toxic digitalis effect The upper record is the control the lower record was made 35 min after intracardiac injection of digitoxin (1 2 mg /kg) Phases 2 and 3 have all but disappeared Recovery is almost entirely based on an increase in the slope of phase 1 These findings are not characteristic for digitalis only and are accompanied by a decrease in overshoot Time lines 0 1 sec

action potential Some of these modifications are associated with alterations in the height and magnitude of resting and of action potentials They correlate therefore with changes in the depolarization process Some of the as yet fairly obscure interrelationships are summarized below

(1) *Changes in concentration of extracellular electrolytes* Increasing extracellular K^+ concentration (decreasing potassium gradient across the membrane) causes a shortening of action potential duration (and a decrease in membrane potential) by decreasing the duration of phase 2 without altering its slope [1, 7] In higher concentration spike formation occurs (TABLE 3) A decrease in external K^+ concentration causes marked prolongation of phase 2 and prolongation and decrease in slope of phase 3 (TABLE 6) After some time the picture reverses completely and shortening with spike formation takes place [17] Na^+ plays its primary role during the early phase of excitation and although changes in Na^+ conductance of the membrane are likely to be concerned with phase 1 and 2 of the recovery process its primary action involves the depolarization process [1, 2, 14, 18] Li^+ may replace Na^+ up to one third of the extracellular Na content [5] When given in higher concentration it causes the standard response increase in phase 1 shortening and steepening of phase 2 and flattening of phase 3 with eventual spike formation Cd^{++} causes a similar response [22] Ca^{++} has different effects on various cardiac tissues and its influence on membrane permeabilities has not been clearly established An increase of Ca^{++} in the extracellular fluid increases the duration of phase 1 and lowers the level of the plateau (phase 2) This produces a record with a pronounced phase 1 reminiscent of the normal pattern for Purkinje fibers upon which Ca^{++} has little effect In the absence of phase 1 (considered an abnormal response for ventricular fibers) Ca^{++} restores the phase and normalizes the pattern (FIGURE 20) When applied in high concentration it causes phase 2 to steepen and phase 3 to lengthen, with an increase in action potential dura

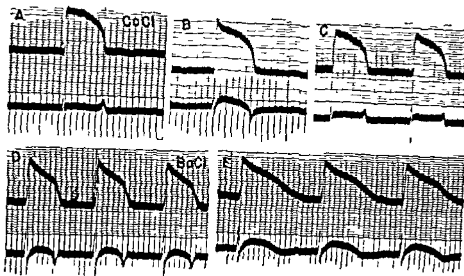


FIGURE 20 Effect of the topical application of Ca^{++} as CaCl on the transmembrane and surface potentials of ventricular fiber (frog) Note in *B* the temporary restoration of phase 1 that is missing in *A* and *C* Striking changes particularly in phase 3 of repolarization may be induced by barium chloride (*F*) with the possible appearance of abnormal T waves and U waves in the surface tracings Similar changes occur during low potassium infusion and in mammalians after veratrine Time lines 0 1 sec

tion[2] Low extracellular Ca^{++} (or the use of calcium chelating agents) converts the triangular configuration of an atrial action potential into a pattern commonly seen in ventricular myocardium with a prolonged plateau of phase 2 The effect of Ba^{++} seems similar to that of low K^{+}, with marked prolongation of phase 2 and an increase in the length and duration of phase 3 (FIGURE 20)[30]

(2) *Changes induced by metabolic inhibitors* The effect caused by changing the extracellular ion concentration has produced a variety of changes practically all ending eventually in the typical spike effect of membrane response The use of a few metabolic inhibitors such as iodoacetic acid[31] 2 4-dinitrophenol and also NaCN has resulted in the kind of response shown in FIGURE 19 This allows little if any interpretation of the metabolic processes concerned with membrane excitation

(3) *Changes induced by various agents and procedures* Anoxia causes the usual shortening and change in slopes 1 2 and 3 in mammalian fibers[32, 3b] but has little effect on preparations of cold blooded animals Acetylcholine causes similar changes in atrial myocardium but affects the ventricular myocardium only in large doses perhaps as the result of irreversible changes (TABLE 5)[2, 18] Digitalis glycosides and strophantin have been mentioned as inciting agents of such spike reaction[32, 3b, 33, 34] In the case of digitalis a statistical analysis has shown a strong correlation between duration of action potential and phase 2 as one would expect and a high negative correlation between duration and slope for phases 1 and 3 ($r = -0.75$ $p < 0.001$) indicating that at least under the influence of these compounds the duration



FIGURE 21 Effects of quinidine gluconate on (1) depolarization time and (2) duration and slope of the recovery phases Note the changes in the width of QRS and in the configuration of T in the surface leads coinciding with the changes in single fiber records The figures denote the width of QRS in seconds Time line 0 1 sec standardization 50 mv

of the two phases changes in opposite directions In a low Ca^{++} surrounding with a shortened action potential duration strophantin restores the normal configuration [35] It is of interest that steroids similar in chemical configuration to the digitalis glycosides have no effect on membrane potentials [35] Alcohol causes the classical spike

On the other hand substances such as quinidine epinephrine and veratrine show a response that is reminiscent of the early effect of low K^+ perfusion and of Ba^{++} with a prolongation of action potential duration and an increase in the length of phases 2 and 3 (FIGURES 20 and 21 TABLE 5) TABLES 3 and 5 list type examples of such a reaction for the ventricular fiber of the frog heart *in situ* with bold figures indicating statistically significant values The measurements were obtained by injection into the vena cava or by topical application and washing TABLE 6 summarizes the early and late events in ventricular fibers following the perfusion of an excised frog heart with K^+ free Tyrode solution that seem to duplicate many of the events discussed above TABLES 7 and 8 summarize some of the known external effects on cardiac transmembrane potentials

Afterpotentials

Following the restoration of membrane resting and action potentials a period of hyper and hypopolarization may be observed usually of relatively short duration and considered comparable to the afterpotentials in nerve In the

TABLE 6
PERFUSION WITH K^+ FREE TYRODE VENTRICULAR FIBER BULLFROG

	C ntr l	E ly	Late
MRP mv	46 4	57 3	66 3
AP mv	73 8	70 3	81 7
AP_d sec	0 54	0 97	0 38
R_S1 mv /sec	394	437	857
R_S2 mv /sec	118	73	637
R_S3 mv /sec	904	186	636

There was no change in depolarization time
Bold type denotes statistically significant values *MRP* membrane resting potential *AP* membrane action potential AP_d action potential duration and R_S1–R_S3 slope of repolarization phases 1 2 and 3

TABLE 7

SUMMARY OF EFFECTS OF CHANGING EXTRACELLULAR ELECTROLYTE CONCENTRATION ON CARDIAC TRANSMEMBRANE POTENTIALS

	MRP	MAP	*OS*	*APd*	*Di*	*Rs1*	*Rs*	*Rs3*	Preparation	Ref
Increase Na^{+}	—	↑	↑	—	—	—	—	—	pDG	1
Decrease Na^{+}	—	↓	↓	—	(↑)	—	—	—	pDG	1
Increase Li^{+}†	—	↓	↓	↓	—	(↓)			vF	28
Increase K	↓	↓		↓	(↑)	(↓)	↓	(↑)	vF	1 16 27 FIGURE 22 TABLE 3
Decrease K^{+}‡	↑	—	—	↑	—	—	↓	↑	vF	1 2 17 TABLE 3
Increase Ba^{+}	—	—	—	↑	—	—	(↑ ↓)	↑	vI	30 FIGURE 20 TABLE 3
Increase Cd^{++}	—	↓	—	↓	—	↓	↓	↑	vI	29
Increase Ca^{++}§	—	—	—	—	—	—	—	—	pC	2 FIGURE 20
						↓	↓	↑	pmC	2 TABLE 3
									avFD	2
Decrease Ca^{++}§	—	—	—	—	—	—	—	—	pCG	23
	—	—	—	↑	—	↑	↑	↓	avD	2
Damage	↓	↓	↓	↓	↑	↓	↓	(↑)	vF	FIGURE 19

Effects on AP_d also shorten the duration of phase 2 of repolarization
† Li may replace Na to some extent
‡ Early effect only
§ Changes threshold potential antagonizes changes following K alteration
—No Change
↑ Higher potential longer duration decreased rate (flatter slope)
↓ Lower potential shorter duration increased rate (steeper slope)
The symbols are as follows p Purkinje fiber pm papillary muscle fiber v ventricular muscle fiber a atrial muscle fiber C cat D dog F frog G goat R rat and Ch chick embryo The other symbols are the same as in TABLE 3

TABLE 8

SUMMARY OF EFFECTS OF VARIOUS PHARMACOLOGICAL AGENTS ON CARDIAC TRANSMEMBRANE POTENTIALS

	MRP	MAP	*OS*	*APd*	*D*	*Rs1*	*Rs2*	*Rs3*	Prep	Ref
Acetylcholine	↓	—	—	↓	↓	—	↓	↓	aF	2 24 25 TABLE 5
	—	↓	↓	↓	—				aR	18
	↑	↓	↓	↓	(↑)	—	—	↑	vCh	9
Epinephrine	—	—	—	↑	—				aR	18
	—	—	—	↓	—	↓	—	↑	vCh	9
Physostigmine	—	—	—	↓	—				aI	18
Carbachol	—	—	—	↓	—				aR	18
Iodoacetate	—	—	—	↓	—	↓	(↓)	↑	vF	31
Digitalis	—	—	—	↓	—	↓	(↑)	↑	vFCh	9 22 33 34 FIGURE 19 TABLE 5
Quinidine	—	—	—	↑	↑	—	↑	↑	pCG	23 FIGURE 21
									vF	TABLES 4 and 5
Procaine†	—	—	—	↑	↑				pCG	23 TABLE 5
Diphenylhydramine	—	—	—	↑	↑				pCG	23
Dinitrophenol‡										
NaCN‡										
Anoxia	↓	↓	—	↓	↑	—	↓	↑	pC	32a
									pmC	
Steroids	—	—	—	—	—	—	—	—	vF	35
Damage	↓	↓	↓	↓	↑	↓	↓	(↑)		

Effects on AP_d also shorten the duration of phase 2 of repolarization
† And other surface anesthetics
‡ Increase diastolic membrane depolarization of the sinus region
The symbols are the same as in TABLES 3 and 7

in situ preparation such changes are not present with any degree of consistency or they may change from beat to beat The usual agents known to cause afterpotentials in nerve[26] do not cause such changes in the myocardial fiber but seem to produce a prolongation of the action potential and a decrease in the slope of phase 3 In the panel on the U wave such changes are discussed in greater detail (pp 942)

General Comments on the Nature of the Membrane as the Seat of Cellular Potentials

The foregoing description reveals large gaps in our knowledge of cellular events in cardiac muscle The observations of a large potential gradient across a membrane can be fully interpreted only if the structure of the membrane is known if its ionic constituents and the ionic concentration differences between the cell the cell membrane the cell boundaries and the cell surroundings have been recognized and if the outward and inward flux of these ions have been determined and the cellular metabolism is understood with respect to certain enzymatic activities controlling cellular entrances and exists A large number of observations on electrical measurements chemical analyses isotope tracer studies and model analogues have now been accumulated and this has laid the groundwork for an interpretation of the nature of an excitable cell and its mode of action Those properties reported for nerve and skeletal muscle have been thought in a large measure to apply to cardiac muscle as well The obvious differences in automatism speed of response and length of recovery that characterize cardiac tissue have posed a number of questions although no one denies that a fundamental similarity exists between all excitable tissues

It may be assumed that the total transmembrane potential (E) is determined by the selective permeability of the membrane to certain ions and that this potential in turn controls some of the selectivity of the membrane toward ionic particles The total transmembrane potential is equal to the sum of the potential changes occurring within the membrane itself (E_M) and the potential changes at the inner (E) and outer (E) interfaces the latter depending on the ionic composition of the adjacent fluids and the distribution coefficients of the ions present

$$E = E + E_M + E \tag{1}$$

This divides the electrophysiological activities still further and invites some general comments on the physical and electrical characteristics of the membrane that separates the external medium from the cellular milieu Naturally these characteristics are interdependent

The membrane with which we are concerned is not the microscopically visible structure that holds a cell together The anatomical cell boundaries are freely permeable to ions and exhibit no special selective powers of molecular transfer The membrane to which we refer is the outer layer of the cellular protoplasm the properties of which differ from the remainder of the cell interior It may be considered paucimolecular varying in thickness within the range of a few molecular layers only This structure has a low surface tension and a low solubility in water characteristics that suggest that layers

of protein molecules are involved[37] The results of X ray diffraction studies comparing lipids lipid mixtures and nerve tissue are also consistent with the assumption that the membrane is a protein structure[38] The low conductivity of the membrane, its wetting properties and other physicochemical characteristics support a concept that a few layers of perhaps radially arranged lipid molecules in more or less liquid form[39] may be part of its internal structure Those who advocate a lipoid character of the membrane assume that a stable film of protein molecules is absorbed on its surfaces and covers the lipoid material The protein macromolecules would be arranged tangentially at the cell surface thus imparting to the membrane its structural solidity Electrical impedance measurements[16] as well as optical studies comparing the light reflecting properties of membranes to those of paucimolecular layers of known diameter[40] suggest a thickness of the membrane of between 50 to 200 Å with 100 Å as the upper limit for lipoid layers alone This corresponds to a membrane thickness of 2 to 4 molecules By comparison the radius of a potassium ion is given as 1 3 Å and that of unhydrated sodium as 0 9 Å[14]

The strong electrical field that exists between an excitable cell and the surrounding area causes the membrane to be polarized that is molecules and molecular layers will orient themselves with positive sided sources and negative sided sinks (electrons and nuclei) so displaced that a *dipole* (source sink) arrangement will be induced within the molecule itself and within the molecular layers The membrane dipole moment (charge × distance) is dependent on the polarizability of the molecule and on the strength of the electrical field[41] Given a transmembrane potential of 0 1 v and assuming a membrane thickness of 100 Å the total potential gradient (E) may be calculated to be of the order of 100 000 v /cm providing that the ionic concentration is equal at the 2 boundaries of the membrane[4] It is likely that this is not the case, and under these circumstances the potential gradient is inversely proportional to ionic concentration If the ionic population on the outside boundary is 10 times that on the inside boundary the potential gradient is 39 000 v /cm on the outside and 390 000 v /cm on the inside of the membrane The magnitude of this electrical field provides strong evidence for membrane polarization with molecular orientation of proteins (enzymes) within its structure Even in the absence of an electrical field a certain amount of polarization may exist because of the number of covalent bonds Such bonds constitute electrical dipoles their strength depending on the difference in electronegativity of the elements forming the bond[41] A quantitative estimation of the dipole moment of the molecular structure of the plasma membrane by Polissar gave values consistent with the assumption that the membrane has a protein structure[4]

These considerations lead to the important statement that if the potential gradient changes membrane polarization is altered and that in consequence molecular orientation of protein macromolecules is disturbed The action of an enzyme for example may depend on the polar orientation of its protein This may determine whether its reactive parts are located within the membrane or are unfolded at its surface In turn this could decide whether the enzyme would or would not react with a given substrate In consequence since the membrane is unstable its physiological properties may be altered profoundly

by changes in transmembrane potentials The function of the membrane is not exclusively determined by polar orientation however since it may be necessary to consider such factors as movement of ions within its structure and changes in the energy stored within the double layers induced by the field[4]

The physical characteristics of the membrane determine its electrical behavior during rest and activity At rest the polarized membrane is a poor conductor with a resistance value between 1 and 2000 ohm/cm² A change in resistance to less than 1 per cent of the resting value occurs on excitation (50 ohm/cm²)[1,2,14,16] On the other hand the capacitance of the membrane remains constant and is independent of rest and activity It measures[1] from 1 (nerve) to 10 (heart muscle) μF/cm² The change in resistance on excitation is related to changes in membrane permeability and accounts for the impulse propagation while the constancy of the capacitance values suggests that a certain skeletal framework of the membrane must remain unaltered during excitation

Transfer of ions across the membrane is likely to be influenced by its molecular structure and by the presence of radicals fixed to the framework of the membrane Depending on the presence or absence of free carboxyl or amino groups such membranes may be considered neutral acid or basic The high selectivity of the membrane may indeed depend on the presence of fixed charges The biological membranes are highly selective to (certain) cations and may therefore be considered acid in character

The factors that determine the magnitude of diffusion potentials for liquid junction boundaries of solutions containing different concentrations of electrolytes separated by a porous membrane have been expressed by Planck (1890) as

$$E = \frac{RT}{nF} \log \frac{U + U}{V - V} \qquad (2)$$

where R expresses the gas constant T the absolute temperature F the Faraday equivalent n the valency of the diffusing ions and U and V the ionic mobilities in water of cations and anions respectively The subscripts denote the two sides of the membrane[43] The Planck equation does not give a specific solution for E_M applies strictly to the resting membrane and does not consider the presence of fixed charges within its structure Assuming a constant potential gradient within the membrane E_M has been defined by Goldman[44] and by Hodgkin and Huxley[15] on the basis of the membrane permeability for Na^+ K^+ and Cl Permeability for an ion j may be expressed as a function of its ionic mobilities the concentration of ions on either side of the membrane and a partition coefficient β_j in the following manner

$$I = \frac{U_j \beta_j RT}{aF} \qquad (3)$$

a being the thickness of the membrane E_M may then be expressed directly as follows[14,15]

$$E_M = \frac{RT}{F} \log \left\{ \frac{P_K(K) + P_N(Na) + P_{Cl}(Cl)}{P_K(K) + P_N(Na) + P_{Cl}(Cl)} \right\} \qquad (4)$$

Experimental values for resting and active nerve (assuming a 500 fold increase in Na permeability on excitation) agree well with the theoretical postulates and provide good evidence for the importance of these ions in the genesis of resting and action potentials An extensive mathematical treatment applied to transmembrane potentials of biological systems on this basis has been given by Johnson, Eyring and Polissar[4]

Whether the membrane has a sievelike structure or may be considered a homogenous layer the resting potential has always been related to differences in ionic concentrations between the cell interior and its external surroundings The magnitude of the resting potential and the ionic composition of the cell interior suggest (1) that the membrane is permeable to cations and to a lesser degree to anions and (2) that specifically for nerve skeletal and heart muscle certain ions, such as K^+ and Cl^- move readily with the potential gradient and in directions opposite from each other Other ions such as Na^+ are blocked from entering This is only approximately true since radioactive tracer studies indicate an exchange of ions in both directions for K^+ as well as for Na^+ during the resting stage[45] The resting membrane then is not impermeable to sodium although Na^+ moves slowly inward and presumably is ejected against the chemical and electrical gradient by an active metabolic process that prevents Na^+ accumulation in the cell interior (the sodium pump)[45, 46] *The difference in the handling of* K^+ *and* Na^+ *by the membrane is of interest* in the light of the known small size of the potassium ion versus a large hydrated Na^+ complex If E were simply a diffusion potential of cations with nondiffusable anion present within the cell a membrane potential of about 12 mv would still be present[4] its selectivity and the presence of the sodium pump are responsible for the higher values The general nature of the processes concerned with ionic movements against the gradient although actually unknown has received a careful detailed analysis by Johnson *et al*[42] Specifically acetylcholine[47] and histamine[48] have been suggested as forming an integral part of the biological system concerned with active ion transport

An external current flow (action current) or a decrease in the activity of certain metabolic processes concerned with membrane selectivity (pacemaker regions) changes the membrane characteristics by decreasing the resting potential to a critical value at which Na^+ (possibly large or hydrated) is allowed to enter the cell at a rapid rate During this time of polarization reversal the pump may or may not be working but whatever has opposed its effectiveness is quickly overcome Na^+ is ejected again and after a characteristic lag K^+ permeability is temporarily increased an outward flux of K^+ counterbalances the Na^+ inflow that preceded it Re establishment of the sodium extruding processes and the K^+ outflow tend to restore the resting potential

It is in these restorative processes that the heart muscle differs from other excitable tissues In cardiac muscle Na^+ flux has not been measured directly but Wilde has demonstrated a pulsatile outflow of K^+ during the cardiac cycle with the peak occurring during the third phase (T wave) of the repolarization process (pp 693) It appears therefore that in heart muscle outward flow of K^+ is delayed and that this may be one of the factors responsible for the slow recovery phases Na^+ expulsion may also occur in a quantitatively different

manner in cardiac fibers Na^+ and K^+ permeabilities may be equal during the plateau phase or one may increase as the other decreases It is even conceivable that the changes in the rate of recovery may depend on the difference in the rate of change at the membrane itself and at its interfaces with the interior and exterior surfaces Most effects so far observed on cardiac muscle fibers have simply been translated in terms of Na^+ and K^+ permeabilities without conclusive evidence in support or to the contrary The other factors mentioned must be considered and it is obvious that further information on the physicochemical structure of the membrane and on the enzymatic action of its constituents is needed before a more meaningful interpretation is possible

Recently some doubts have been raised concerning the assumption that the membrane potentials are simply related to the ratio of ionic concentration on either side of the membrane since microinjections of ions into the interior of the giant axon of the squid have failed to produce the changes to be expected if the membrane resting potential involved the mechanism of some type of Donnan potential[7, 62] Whatever the interpretation of these findings[60] they strengthen the view that complex phenomena within the membrane itself including the active sodium extruding process play a decisive part in the observed potential

The question has also been raised as to whether mitochondria considered the seat of cellular respiration and oxidative phosphorylation may also be concerned with ionic distribution within and without the cell[61] Recent studies have suggested a certain partition of effects Na^+ and K^+ movements during rapid changes in membrane resistance do reflect changes in the properties of the membrane itself while the more subtle adjustments during the recovery phase and during the time the membrane is at rest may depend on the metabolic action of mitochondria Agents that affect directly and rapidly the transfer of K^+ and Na^+ such as cholinergic compounds and digitalis have no effect on the ion transfer of isolated mitochondria while the action of metabolic inhibitors (dinitrophenol fluoroacetate) seems to depend upon the metabolic properties of these cellular organelles[5]

The Relation of Membrane Potentials to Surface Events

With the exception of ingenious experiments on myelinated nerve fibers[63] extracellular records cannot give precise information on the nature of the cellular state although it is obvious that the changes in surface potentials are to a large degree dependent upon it Depolarizing an area by injury and recording from injured to intact fiber has frequently been done however in an attempt to obtain information on the nature of intracellular changes and on the influence of various agents and procedures on cellular metabolism Much of the earlier work concerned with such demarcation potentials has been summarized in Schutz s monograph[64] Because of the cellular short circuits caused by the injury such potentials are never as large as true membrane potentials The relation of the injury potential E to E the over all membrane potential may be expressed as

$$E = \frac{R_o}{R_o + R_M} E \qquad E = E \; \frac{R_o + R_M}{R_o} \qquad (5)$$

with R and R_M expressing external and internal resistance values, respectively. This equation shows that the injury potential is a fraction of the transmembrane potential depending on resistance ratios and that the presence of injury must alter the cellular potential. Stated differently, a surface electrode P records a surface potential V as a function of (1) the dipole moment of the fiber M, (2) the angle of observation θ (expressing the location of the electrode with respect to the direction of the dipole moving over the fiber) and (3) the distance of P from the fiber according to the familiar Helmholtz equation

$$V = M \frac{\cos\theta}{r^2} \tag{6}$$

with the second term on the right equivalent to the solid angle Ω subtended at the electrode by the (injured) surface. If P is placed on the axis of the cell fiber in contact with the injured surface, the second term is reduced to 2π and V equals $M2\pi$. The potential within the fiber is given as $M4\pi$.[55] In consequence, the injury potential is related to, but can never exceed or even approach the true membrane potential. Actual comparisons on skeletal muscle have shown the injury potential to be at best 60 per cent of the true cellular po

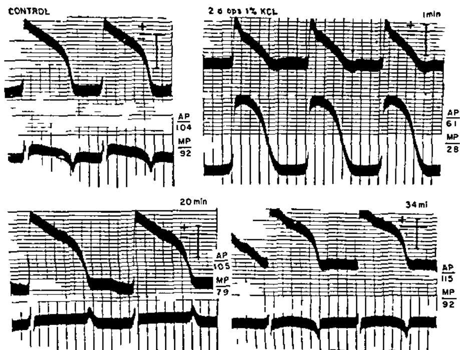


FIGURE 22. Transmembrane and injury potential following topical application of KCl (frog ventricular muscle *in situ*). Note the qualitative difference between the two monophasic records which were obtained less than 1 mm apart and the changes in the T wave on recovery. Standardization 50 mv. AP: action potential. RP: resting potential.

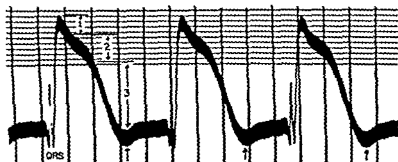


FIGURE 23 C D a seven year old child with congenital heart disease endocardial electrocardiogram from the right ventricle Time 0 1 sec Phases 1 2 and 3 are indicated the arrow points to hyperpolarization.

tential[56] Qualitative differences may also exist since the observed injury potential is always the net resultant of the effect of injury on many fibers Striking differences in configuration between the two types of curves recorded within a millimeter of each other are illustrated in FIGURE 22, which was obtained after the topical application of KCl Conclusions based on injury effects both with respect to cellular potentials as well as to the nature of surface effects have to be accepted with caution

On the other hand such potentials do at times simulate true cellular events This may lead to the erroneous assumption that any monophasic record obtained with a small electrode may represent a transmembrane potential FIGURES 23 and 24 demonstrate an injury effect induced in a human subject by an electrode incorporated into a cardiac catheter The catheter was passed through the venous system into the right ventricle and the electrode was made to touch the ventricular myocardial wall The injury potential that was produced demonstrated many characteristics of an intracellular recording including three separate recovery phases hyperpolarization and evidence of overshoot when the electrode was withdrawn (FIGURE 24) Almost the only

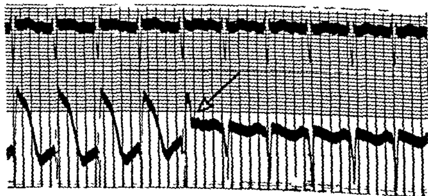


FIGURE 24 Same as in FIGURE 23 At the arrow the catheter has been withdrawn revealing overshoot The upper tracing has a simultaneous lead V as control

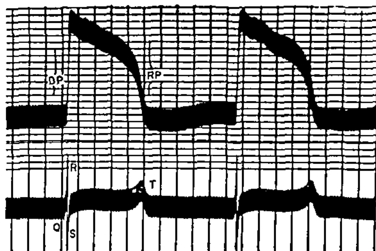


FIGURE 25 A normal cardiac transmembrane potential and its relation to the surface electrocardiogram DP depolarization RP repolarization Time lines 0 1 sec

discriminating feature between records of this type and true cellular potentials is the presence of an unbroken depolarization in the transmembrane record Injury potentials generally show the effects of an advancing dipolar surface excitation with its characteristic spike or at least with an abortive spike (notching and slurring)

Of more general interest is the relationship of transmembrane potentials to the uninjured surface electrograms and indirectly to the surface electrocardiogram recorded at a distance from the heart FIGURE 25 demonstrates that depolarization reversal of polarization and phase 1 of recovery coincide with the surface QRS that the final phase 3 occurs simultaneously with the surface T wave and that the plateau (phase 2) corresponds to the ST segment The sharp fall in membrane resistance that coincides with excitation causes a current to flow *across* the fiber (from without inward) The decrease (or reversal) of polarization of the excited region initiates a current flowing *along* the fiber from the resting (polarized) segment the source into the active segment the sink By this process the resting potential of a fiber adjoining an excited region is reduced and in turn will depolarize as soon as a critical decrease in resting potential has occurred This causes the next fiber to fire in a continuation of the reaction resulting in the well described succession of sources followed by sinks moving over the tissue This chain reaction the action current is related to the rate of polarization reversal but not to the magnitude of the resting and action potentials

Pronounced changes in the absolute magnitude of cellular potentials have indeed no influence on the configuration of surface events except in so far as the resting potential itself influences the depolarization process (pp 672) As an expression of the rate of change of cellular potentials the surface electrocardiogram could be considered the first derivative of the total membrane

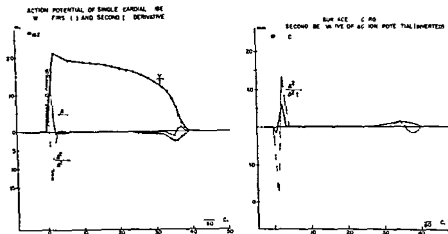


FIGURE 26 Surface records as the first and second derivative of transmembrane potentials

potential $I = \frac{\Delta E}{\Delta t}$ (FIGURE 26) Calculating or electronically recording the first derivative from the monophasic membrane potential yields a simple biphasic curve with a positive (QRS) and negative (T) component and represents the type of records that may be obtained from isolated muscle strips suspended in air On the other hand in a volume conductor with the preparation submerged in conducting fluid experimental observations and calculations based on the laws that govern the distribution of currents in such media have yielded multiphasic curves with a characteristic plus minus deflection at the beginning of excitation [55, 57] FIGURE 27 demonstrates the similarity between a theoretically constructed curve and a surface record obtained from atrial tissue in contact with a catheter electrode in man [57] Such records are related much more closely to the second derivative of the membrane potential (FIGURE 26) The theory of transmission of electric currents through cables postulates that the transmembrane voltage in such a structure is proportional to the second derivative of the current flowing through the membrane

$$\frac{\Delta E}{\Delta x^2} = -(r + r) I_M \quad (7)$$

with r and r defining the resistance of the outer and inner circuits and I_M the membrane current The cable theory has been successfully applied to nerve conduction [16] but whether a similar analysis is applicable to the syncytial network of cardiac musculature has yet to be determined One may state however that at least in a qualitative sense the surface potentials of the heart, when suspended in a conducting medium are proportional to the membrane current Assuming that surface records represent membrane current curves monophasic complexes could be reconstructed by double integration (the re

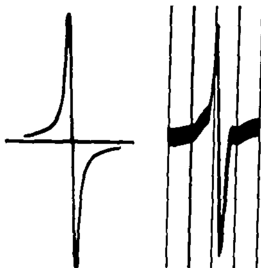


FIGURE 27 Constructed surface electrocardiogram on the left compared to an intracardiac recording from an interatrial septum in man (QRS complexes only) Note the similarity between the calculated and the recorded event (Hecht and Woodbury[57])

verse process of FIGURE 26) which in configuration closely resemble the various transmembrane potentials we have demonstrated[58]

Substances that depress conduction and decrease the speed of impulse propagation do so by virtue of their effect on membrane current which is indicated by a change in the rate (slope) of depolarization as demonstrated in the case of QRS changes following quinidine administration Substances that decrease the magnitude of the resting potential may eventually affect the rate of depolarization and thereby may affect impulse propagation as well as in the end stages of hyperpotassemia with a widening of QRS Alterations of the RT junction and the RST segment may be related to changes in the first phase of recovery of which the surface changes induced by digitalis and anoxia represent examples T wave changes proper are associated with modifications in the duration and slope of the final recovery process (phase 3) which is particularly sensitive to changes in external potassium concentration (characteristic T wave changes in states associated with high and low levels of extracellular potassium)

Obviously the configuration of a surface electrocardiogram is also determined by a great variety of external factors that influence the distribution of currents in inhomogeneous volume conductors of finite extent In addition *these currents must at all times be considered as the resultant of all fibers undergoing* excitation and recovery at a given time and they are dependent to some extent on the difference in duration of the action potentials of fibers located within different areas of the myocardium Many of these changes find their eventual expression in terms of a detailed analysis of the transmembrane potentials of the individual myocardial fiber

Acknowledgments

I am deeply indebted to my many associates and students for continued stimulation and assistance I am particularly grateful to A Brady R P Carlisle J Heath G Hickman W A Jenkins E Maier C V Nelson A S Ruby Lowell A Woodbury and J Walter Woodbury

References

1 WEIDMANN S 1956 Elektrophysiologie der Herzmuskelfaser Sammlung innere Medizin und ihre Grenzgebiete 4 Huber Bern Switzerland

2 BROOKS C M B HOFFMANN E E SUCKLING & O ORIAS 1955 Excitability of the Heart Grune & Stratton Philadelphia Pa

3 WOODBURY L A H H HECHT & A R CHRISTOPHERSON 1951 Membrane resting and action potentials of single cardiac muscle fibers of the frog ventricle Am J Physiol 164 307

4 WOODBURY J W & A J BRADY 1956 Intracellular recording from moving tissues with a flexibly mounted ultramicroelectrode Science 123 100

5 BERNSTEIN J 1912 Elektrobiologie Die Wissenschaft Vieweg Braunschweig Germany

6 BOYLE P J & E J CONWAY 1941 Potassium accumulation in muscle and associated changes J Physiol 100 1

7 GRUNDFEST H 1955 The nature of electrochemical potentials of bioelectric tissues 141 *In* Electrochemistry in Biology and Medicine T Shedlovsky Ed Wiley & Son New York N Y

8 NELSON C V & H H HECHT 1955 The resultant electrical dipole moment of the frog heart Am J Physiol 183 647

9 FINGL, E L A WOODBURY & H H HECHT 1952 Effects of innervation and drugs upon direct membrane potentials of embryonic chick myocardium J Pharmacol 104 103

10 TRAUTWEIN W U GOTTSTEIN & K FEDERSCHMIDT 1953 Der Einfluss der Temperatur auf den Aktionsstrom des excidierten Purkinje Fadens gemessen mit einer intracellularen Elektrode Pflugers Arch ges Physiol 258 243

11 CORABOEUF E & S WEIDMANN 1954 Temperature effects on the electrical activity of Purkinje fib es Helv Physiol et Pharmacol Acta 12 32

12 TRAUTWEIN W & J DUDEL 1954 Aktionspotential und Mechanogramm des Warmbluterherzmuskels als Funktion der Schlagfrequenz Pflugers Arch ges Physiol 260 24

13 BRADY A J & H H HECHT 1953 Membrane and action potential of single cardiac muscle fibers during ventricular fibrillation Federation Proc 12 19

14 HODGKIN A L 1951 The ionic basis of electrical activity in nerve and muscle Biol Revs Cambridge Phil Soc 26 339

15 HODGKIN A L & A F HUXLEY 1952 Movement of sodium and potassium ions during nervous activity Cold Spring Harbor Symposia Quant Biol 17 43

16 COLE K S 1955 Ions potentials and the nerve impulse 121 *In* Electrochemistry in Biology and Medicine T Shedlovsky Ed Wiley & Son New York N Y

17 HECHT H H J HEATH & E MAIER Unpublished observation.

18 WEBB J L & P B HOLLANDER 1956 The action of acetylcholine and epinephrine on the cellular membrane potentials and contractility of rat atrium Circulation Research 4 332

19 HOFFMAN B F & E E SUCKLING 1952 Cellular potentials of intact mammalian hearts Am J Physiol 170 357

20 TRAUTWEIN W & K ZINK 1952 Über Membran und Aktionspotentiale einzelner Myokardfasern des Kalt und Warmbluterherzens Pflugers Arch ges Physiol 256 68

21 BURGEN A S V & K G TERROUX 1953 The membrane resting and action potentials of the cat auricle J Physiol 119 139

22 WOODBURY L A & H H HECHT 1952 Effects of cardiac glycosides upon the electrical activity of single ventricular fibers of the frog heart, and their relation to the digitalis effect of the electrocardiogram Circulation 6 172

23 WEIDMANN S 1955 Effects of calcium ions and local anaesthetics on electrical properties of Purkinje fibres J Physiol 129 568

24 del Castillo J & B Katz 1955 Production in membrane potential changes in the frog heart by inhibitory nerve impulses Nature 175 1035
25 Hutter O F & W Trautwein 1955 Effect of vagal stimulation on the sinus venosus of the frog s heart Nature 176 512
26a Brady A J & H H Hecht 1957 Resting membrane and action potentials of the spontaneously beating pacemaker region of the perfused turtle heart Circulation Research In press
26b Brady A J & H H Hecht 1954 On the origin of the heart beat Am J Med 17 110
26c Brady A J 1952 Membrane resting and action potentials of the cardiac pacemaker of the turtle Thesis Univ Utah Salt Lake City Utah
27 Weidmann S 1956 Shortening of the cardiac action potential due to a brief injection of KCl following the onset of activity J Physiol 132 157
28 Stein E M Kleinfeld H Greene & S Meyers 1955 Action of lithium chloride on the isolated perfused frog heart Am J Physiol 183 121
29 Kleinfeld M H Greene E Stein & J Magin 1955 Effect of the cadmium ion on the electrical and mechanical activity of the frog heart Am J Physiol 181 35
30 Kleinfeld M E Stein & S Meyers 1954 Effects of barium chloride on resting and action potentials of ventricular fibers of the frog Circulation Research 2 488
31 Kleinfeld M E Stein J Magin & C Kossmann 1955 The action of iodoacetate on the electrical and mechanical activities of the isolated perfused frog heart J Clin Invest 34 1802
32a Trautwein W U Gottstein & J Dudel 1954 Der Aktionsstrom der Myokardfaser im Sauerstoffmangel Pflügers Arch ges Physiol 260 40
32b Conn H L 1956 Effects of digitalis and hypoxia on potassium transfer and distribution in the dog heart Am J Physiol 184 548
33 Trautwein W & P N Witt 1952 Der Einfluss des Strophanthins auf das Ruhe und Aktionspotential der geschädigten Herzmuskelfaser Arch exptl Pathol Pharmakol 216 197
34 Stutz H E Feigelson J Emerson & R J Bing 1954 The effect of digitalis (Cedilanid) on the mechanical and electrical activity of extracted and nonextracted heart muscle preparations Circulation Research 2 555
35 Woodbury L A & H H Hecht 1952 Effects of some steroids on membrane potentials of single ventricular fibers of frog heart Federation Proc 11 175
36 Dawes G S 1952 Experimental cardiac arrhythmias and quinidine like drugs Pharmacol Revs 4 43
37 Davson H & J C Danielli 1952 The Permeability of Natural Membranes Cambridge Univ Press New York N Y
38 Schmitt F O & K J Palmer 1940 X Ray diffraction studies of lipids and lipid protein systems Cold Spring Harbor Symposia Quant Biol 8 94
39 Chambers R & M J Kopac 1937 The coalescence of living cells with oil drops J Cellular Comp Physiol 9 331 345
40 Waugh D F & F O Schmitt 1940 Investigation of the thickness and ultrastructure of cellular membranes by the analytical leptoscope Cold Spring Harbor Symposia Quant Biol 8 233
41 Glasstone S 1946 Textbook of Physical Chemistry 2nd ed D Van Nostrand New York N Y
42 Johnson F H H Eyring & M J Polissar 1954 The Kinetic Basis of Molecular Biology Wiley & Sons New York N Y
43 McInnes D A 1939 *The Principles of Flectrochemistry Reinhold New York* N Y
44 Goldman D E 1942 Potential impedance and rectification in membranes J Gen Physiol 27 37
45 Keynes R D 1951 The ionic movements during nervous activity J Physiol 114 119
46 Dean R B 1941 Theories of electrolyte equilibrium in muscle Biol Symposia. 3 331
47 Nachmansohn D & I B Wilson 1955 Molecular basis for generation of bioelectric potentials *In* Electrochemistry in Biology and Medicine 167 T Shedlosky Ed Wiley & Sons New York N Y
48 Eyring H & T F Dougherty 1955 Molecular mechanisms in inflammation and stress Am Scientist 43 457
49 Shar? F H S E Simon & B M Johnstone 1956 The non-correlation of bioelectric potentials with ionic gradients. J Gen Physiol 40 1

50 Hodgkin A L & R D Keynes 1956 Experiments on the injection of substances into squid giant axons by means of a micro syringe J Physiol 131 592
51 Bartley W R E Davis & H A Krebs 1956 Active transport in animal tissues and sub-cellular particles Proc Roy Soc London B142 187
52 Holland W C & C F Dunn 1954 Role of the cell membrane and mitochondria in the phenomenon of ion transport in cardiac muscle Am J Physiol 179 486
53 Huxley A F & R Stampfli 1951 Direct determination of membrane resting and action potential in single myelinated nerve fibers J Physiol 112 476
54 Schutz F 1936 Elektrophysiologie des Herzens bei einphasischer Ableitung Ergeb Physiol Biol Chem u exptl Pharmakol 38 493
55 Wilson F N A G Macleod & P S Barker 1933 Distribution of the current of action and injury displayed by heart muscle and other excitable tissues Univ Mich Press Ann Arbor Mich
56 Rothschuh K E & H Meier 1954 Experimentelle Untersuchungen über das Membranruhepotential das Verletzungspotential und das Kernhüllen Widerstandsverhältnis am M sartorius Z Biol 107 264
57 Hecht H H & L A Woodbury 1950 Excitation of human auricular muscle and the significance of the intrinsicoid deflection of the auricular electrocardiogram Circulation 2 37
58 Churney L R Ashman & E Byer 1948 Electrogram of turtle heart strip immersed in a volume conductor Am J Physiol 154 241

DISCUSSION PART I

Kenneth S Cole *Chairman*

WILLIAM I NASTUK (*Department of Physiology Columbia University, New York N Y*) I believe that the first question to be considered has been suggested by Kenneth S Cole To what extent do the relations that describe so well the membrane behavior of the squid axon apply to cardiac muscle membranes? I shall begin by comparing some salient features of each

In the squid axon impulse propagation begins with a passive depolarization of the membrane As the membrane potential difference is reduced sodium ion entry increases aiding the passive depolarization When the membrane potential reaches a critical level the magnitude of the sodium ion inrush is such that the depolarization process becomes self sustaining and it is at this moment that a propagated action potential originates The sodium ion inrush increases still further and then rapidly wanes During the period of sodium ion inflow the potassium ion outflow also increases but more slowly The peak in potassium ion outflow occurs about 0 5 msec later than the peak in sodium ion inflow and the two processes are displaced in time It is the early rise in sodium ion inflow that reduces the membrane potential and it is the delayed rise in potassium ion outflow that restores the membrane potential to the value found in the resting cell

On comparison, the cardiac muscle fiber behaves like the squid axon in certain respects Pertinent to the initiation of activity S Weidmann has pointed out that a passive reduction of membrane potential in the Purkinje fiber when carried to a critical level sets up a propagated action potential At the pace maker site this triggerlike reduction in membrane potential occurs spontaneously

A point that seems well established is that the rising phase of the action potential in the cardiac muscle fiber results from an increase in its permeability to sodium ions Support for this mechanism is provided by experiments in which the extracellular sodium ion concentration is varied The changes in maximum active membrane potential that result are in close agreement with predictions based on the relative sodium ion concentrations in the intracellular and extracellular fluids

Following the peak in the cardiac fiber action potential there is a long lasting recovery phase during which the electrical resistance of the membrane first rises The resistance is later reduced at a time when the membrane potential is approaching the resting level These peculiarities of the recovery process might be explained on the basis of a delayed rise in potassium ion permeability In other words for the cardiac fiber the transient increases in sodium ion and potassium ion permeabilities are separated by a longer time interval than is the case in the squid axon

In discussing this point Weidmann described the effects produced by application of anodic current and by increased extracellular potassium ion concentration in so far as they trigger and hasten membrane recovery in active cardiac

fibers He offered three possible explanations for these results namely increased sodium pumping decreased sodium permeability or increased potassium permeability Clearly further experimental work is necessary in order to settle this important matter

For the second question I might begin by asking what kind of alteration in membrane properties is required to explain the time sequence of permeability changes that occur during impulse conduction We all know that acetylcholine has been thought to be an agent that reacts with the resting membrane thereby producing alterations in its structure These changes lead to increased ionic permeability and the ensuing transmembranal ionic movements shift the membrane potential

It is possible to show that the membrane potential of a skeletal muscle fiber is reduced in the vicinity of the end plate if acetylcholine is applied topically to this zone In this connection one might expect to be rewarded with some general information on the mode of action of acetylcholine if the depolarization phenomenon at the end plate could be more fully understood

From a study of the electrical behavior of muscle cell membranes at the end plate during neuromuscular transmission Fatt and Katz (1951) suggested that during such transmission the end plate membrane becomes permeable to all species of ions They described the membrane in this state as short circuited and it is interesting to recall that this state is like that proposed by J Bernstein many years ago to explain the propagation of an action potential along an axon It is generally agreed that neuromuscular transmission in vertebrate muscle is mediated via released acetylcholine and that therefore the term short circuited describes the behavior of the end plate membrane under the influence of acetylcholine In passing it may be worthwhile to mention that the situation described as a short-circuited end plate where the rise in membrane permeability is simultaneous for all ion species is not comparable to that existing when sequential and selective rises in ionic permeability occur during impulse propagation in the squid axon

The effect of acetylcholine on the electrical behavior of cardiac fibers has been studied by several groups of investigators Burgen and Terroux (1953) applied acetylcholine to cat auricle and showed that the membrane resting potential was *increased* They also showed that under these conditions the duration of the action potential shortened and that repolarization occurred earlier It is also interesting to note that the mechanical response of the muscle was diminished both in amplitude and duration Hoffman and Suckling (1953) studied membrane potentials in auricular fibers of the dog and found that both vagal stimulation and acetylcholine application increased the rate of membrane repolarization but neither treatment had any effect on the magnitude of the resting and action potentials

The investigators del Castillo and Katz (1955) and Hutter and Trautwein (1955) have performed essentially the same experiment that is one involving the recording of transmembrane potentials from fibers in the sinus venosus of the heart of the frog before during and after vagal stimulation The interesting finding here is the fact that vagal stimulation results in a hyperpolarization

of the membrane and if stimulation is vigorous a complete stoppage of the pacemaker activity In the period after stimulation the first action potential that arises spontaneously shows a diminished overshoot and a faster rate of repolarization compared with the control

I point out the preceding facts to show that the action of acetylcholine on membranes is far from completely understood A good illustration is the directly opposite effect of acetylcholine on membrane potentials at the pace maker site in auricular tissue and on the end plate of the skeletal muscle fiber This behavior may mean that these membranes differ in some important funda mental way

I should like to conclude by adding that the results of modern investigations such as those to which I have referred and others not mentioned have it seems to me made the teaching of cardiac electrophysiology much more pleasant and meaningful than it has been in the past

References

BURGEN A S V & K G TERROUX 1953 J Physiol 120 449
DEL CASTILLO J & B KATZ 1955 Nature 176 1035
FATT P & B KATZ 1951 J Physiol 115 320
HOFFMAN B F & E E SUCKLING 1953 Am J Physiol 173 312
HUTTER O F & W TRAUTWEIN 1955 Nature 176 512

H EYRING (*University of Utah Salt Lake City Utah*) It seems to me that the speed of potential rise at the beginning of the resting state measures merely the speed at which purely electrical processes can occur In the recovery process on the other hand we are not seeing electrical changes as the slow process but as the chemical effects Is this not so? It seems to me that when cardiac glycosides speed the recovery of the resting potential of cells they must do this by stabilizing the resting state or else by speeding up the outward po tassium current Is it not true that we are observing the effect of chemical changes on rates as much as we are studying electrical conduction?

K S COLE (*National Institutes of Health Bethesda Md*) The change of potential during the excitatory phase obviously must be governed by the rate at which ions can get through since we do not expect to be either generating or destroying them and that rate will depend upon their number and the speed at which they can travel Similarly the recovery will be governed by the motion of the net charge in the other direction To rephrase your question I should like to ask if the excitatory phase may be limited only by the ability of the membrane to carry ions that are present whereas the more complex and in general slower phenomena of the recovery phase may be limited bv the proc ess by which ions are made available or by other essentially chemical processes in the membrane?

H EYRING One could speculate on the activity of the digitalis glycosides They presumably help the heart by shortening the long recovery period during which metabolites present in short supply in the weakened heart are being consumed It is interesting that the digitalis glycosides although themselves steroids which superficially resemble the various hormones from the adrenal

cortex, are still so specific for heart mu cles It appears that the steroids, like most of the local anesthetics tend to stabilize the resting state of various types of cells

H Eyring Can we agree that chemical processes change the permeabilities during the recovery?

S Weidmann (*University of Berne Berne Switzerland*) I am certain they do but ionic movement is necessary to bring about potential changes

H Eyring I am sure that is correct

A M Shanes (*Laboratory of Pharmacology and Toxicology National Institute of Arthritis and Metabolic Diseases National Institutes of Health Bethesda Md*) I should like to ask Weidmann three distinct questions First do you know the magnitude of the resting potential in the quiescent state and in the fluctuant state what is the size of the action potential? Second when potassium is injected is there any indication of its effect on the conductance of the membranes? Finally what effect does the metabolic inhibition have on the time course of the action potential assuming it is possible to maintain the resting potential during metabolic inhibition?

S Weidmann The first question is easily answered and has been treated by Hans Hecht Regarding your second question the effect of potassium I am not aware of any relevant findings One should measure K^{+} influx and outflux at different extracellular K concentrations possibly with a turtle ventricle perfused through its coronary artery

A M Shanes How about electrical measurement?

S Weidmann Very little change indeed astonishingly little I have depolarized cardiac fibers with isotonic potassium chloride to about 10 mv and have thereby lowered the resistance by a factor of 2 but not more

A M Shanes And my third question?

S Weidmann Metabolic inhibition shortens the action potential before the resting potential drops appreciably

C E Kossmann (*New York University College of Medicine New York N Y*) It is an interesting tribute to the inclusiveness of this monograph and the encompassing vision of its Consulting Editor that contributors to this section have included an axonologist an electrophysiologist a physical chemist a physiologist a clinical investigator and now one who regards himself as primarily a clinician

That the technique of recording intracellular potentials should be utilized at this stage or at any stage of its development by the clinical investigator or the clinician may be viewed with considerable alarm and rightfully by those basic scientists already represented in these pages who have devoted a very considerable portion of their lives to such matters When however we consider the frustration inherent in the unsuccessful treatment of the numerous abnormalities of cardiac function that are encountered daily by the clinician perhaps we shall understand the clinician s driving urge to utilize the technique of intracellular potentials in an attempt to solve some of the problems of dy

function caused by disease. I think we could argue from the information included in this monograph that if the knowledge of the origin of the normal transmembrane potential is still incomplete the study of tissue made abnormal by manipulation or disease can have little meaning. Medical science is replete, however, with examples of useful investigations carried on in disease when the normal physiology of the situation was poorly or incompletely understood. The very method about which this monograph revolves, the electrocardiographic method, is an example. We have used it in the clinic with reasonable accuracy for half a century, yet later on in these very pages we shall still be arguing *about how excitation spreads through the normal ventricles!*

Our problem has been a simple one and perhaps we have been a little naive. We have been trying to make estimates of the mechanical behavior of the heart from an electrical record. In the clinic it is easy to make an electrical record but it is difficult to make a direct measure of mechanical activity such as cardiac output. With this restriction in mind we have considered the intracellular potential, not altogether willingly, but in an effort to bridge the gap between normal membrane function and clinical medicine.

FIGURE 1 will give you some idea of the lines along which we have been

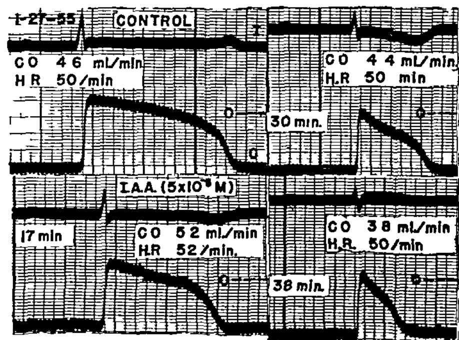


FIGURE 1. Effect on the frog heart of 5×10^{-5} M iodoacetate administered in frog Ringer's solution. The simultaneous records are of the indirect electrocardiogram above (I gain 1 0 cm = 1 mv) and the intracellular potential of a ventricular cell below (C gain 0 9 cm = 50 mv). Cardiac output and heart rate were measured just before recording the potentials in each instance. All measurements were made from the top of the trace, and the dotted line indicates the zero level of potential (0) of the membrane. Note the considerable change in the duration of the action potential before cardiac output is impaired.[1]



FIGURE 2 Simultaneous bipolar external lead (I upper records) and ventricular intracellular lead (C_P lower records) in the frog modified by the intra aortic injection of 0 3 mg of triiodothyronine Note in record B the alternation in the slope of the recovery process of the presumed after potential and of the comparable deflections in the bipolar leads In the intracellular record the small deflection preceding the ventricular action potential is an artefact probably caused by atrial systole In C the alternation has subsided

injury of the endocardium did not slow ventricular activation to a greater extent than did simple incision into the area of the left bundle branch The ventricular septum was activated from apex to base and the mean septal vector was of considerable magnitude but ordinarily was apparently negated by the free wall activation occurring simultaneously In some cases at least endocardial activation approached somewhat the same pattern after an induced left bundle branch block Of interest also are the early potentials preceding the muscle potential proper by 8 to 12 msec that may be encountered in the left upper septum [4]

References

1 LEWIS T & M A ROTHSCHILD 1915 The excitatory process in the dog s heart Part II The ventricles Phil Trans Roy Soc London B 206 181–226

2 PRUITT R D H E ESSEX & H B BURCHELL 1951 Studies on the spread of excitation through the ventricular myocardium Circulation 3 418–432

3 BURCHELL H B H E ESSEX & R D PRUITT 1952 Studies on the spread of excitation through the ventricular myocardium II The ventricular septum Circulation 6 161–171

4 BURCHELL H B H E ESSEX & F H LAMBERT 1953 Action potentials supporting the presence of specialized conduction pathways in the dog s ventricle Abstr Circulation Research 1 186–188

THE GENERAL ORDER OF EXCITATION AND OF RECOVERY

By Hans Schaefer
University of Heidelberg Heidelberg Germany

The use of the word general in the title of this paper indicates that only the basic principles of our present concepts concerning excitation and recovery will be outlined There is of course the temptation to venture into regions of pure speculation with the danger that most of the expressed concepts may later lose validity in the light of grim facts Let us therefore attempt to combine considerations of more or less theoretical character with a factual presentation of details describing the process of excitation and of recovery of the cardiac muscle

Technical Aspects of Exploring the Excitation Process

Several techniques have been developed for the exploration of the excitation process We all are familiar with the old and famous concept of Lewis and Rothschild (1915) which describes in a surprisingly correct manner the time course of the excitation wave over ventricular musculature This picture however was obtained by using the so called unipolar leads In consequence its validity is based upon the assumption that intrinsic deflection is a correct indicator of the time of local activation Obviously this is true only within rather large limits of error We know that the beginning of the downstroke in the exploring electrode by no means coincides with the beginning of local depolarization (Durrer and van der Tweel 1954 Schaefer 1950 Schaefer and Trautwein 1951 Sodi Pallares *et al* 1950 1955 Veyrat 1953 Wilson *et al* 1947) As will be seen in FIGURES 1 and 2 sometimes there are considerable differences between the onset of the local process as recorded with narrow (<1 mm) bipolar electrodes and the beginning of the downstroke in a unipolar lead from the surface of the heart as recorded by one of the bipolar electrodes and by a Wilson central terminal (CT) We therefore consider it necessary to record local latencies with bipolar electrodes only and we are in agreement with nearly all modern investigators in this respect In consequence any unipolar exploration of intramural events creates some serious difficulties the most important being the lesion of muscle fibers caused by the insertion of needle electrodes The brilliant investigations of Scher Sodi Pallares Prinzmetal Durrer and their collaborators reported elsewhere in these pages show how these difficulties eventually have been overcome When my associates and I started this work in 1947 we used for reasons mentioned bipolar surface electrodes with a very small distance (0 15 to 0 3 mm)

Such local derivations are scarcely applicable to human hearts at least not as a routine technique Groedel and Borchardt (1948) succeeded in recording unipolar electrocardiograms (ECGs) from the human heart surface but their results are not suitable for an exact analysis of the spread of excitation waves because of the above mentioned difficulties in the interpretation of an intrinsic deflection Moreover information in the case of human subjects must be

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application leads to a theory derived from the ECG that interprets the form of the ECG waves in terms of the spatial and time order of events in the various elementary fiber units of the myocardium. Such a theory is based on the vector concept. If every fiber produces an electrical field with any distortions whatsoever and if there exists an effect of independent superposition of these individual fields with as many restrictions concerning accuracy as may be desired, the model that best describes the time course of the ECG is vectorial in character. I think this conclusion is now widely accepted in spite of certain sharp attacks made by a number of workers in Germany (Ernsthausen and Kienle, 1953; Kienle, 1955). The very careful experiments of American (Frank, 1955; Levine *et al.*, 1953; Schmitt *et al.*, 1953; Simonson *et al.*, 1953)

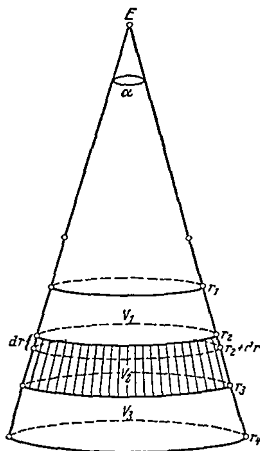


FIGURE 3. Equivalence of muscle masses producing action potentials. E is the exploring unipolar electrode and α is the solid angle under which the muscle appears from the electrode. The muscle may have a diameter from r_1 to r_4 and may lie between the spheres symbolized by their cross sections with the angle α. The center of all spheres is E. If all fibers are oriented at a random order and of homogeneous distribution throughout the muscle, their potentials are equivalent if the products of their diameters—r_1r_2, r_2r_3, r_3r_4—and of the angle under which the masses appear from E are equal (Schaefer, 1951).

and French authors (Jouve *et al* 1953 Meyer *et al*, 1955) of Duchosal and Sulzer (1949) Hartmann *et al* (1955) and those made in our own laboratory (Baust *et al* 1954 Bock and Baust 1954 Bock *et al*, 1954 Dohrmann 1954) certainly strengthen our belief that the vector concept is an adequate but certainly by no means an absolutely accurate means of describing the sum of all electrical events in the heart. The validity of this concept is based mainly on the following assumptions:

(1) All records of the ECG with various lead positions are predictable with sufficient accuracy from one spatial vector loop (Duchosal and Sulzer 1949)

(2) In spite of the relatively great diameter of the heart mass it is possible to determine an electrical center of gravity by the mirror pattern method namely by the cancellation technique

(3) The insertion of artificial dipoles into the heart of living or dead bodies leads to the same errors in predicting the shape of dipole potential as in predicting the ECG from various electrode positions from one definite vector loop (FIGURE 4)

(4) A fourth argument the first in the history of ECG is nevertheless the

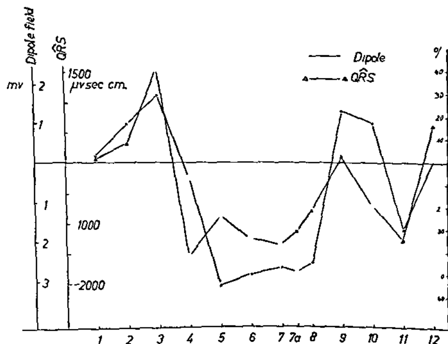


FIGURE 4 Deviation of the recorded local unipolar potential from the expected magnitude. The measurements were obtained from an experiment on a dog with an artificial dipole inserted into the right cavity. The potentials have been calculated from the usual dipole equations. The abscissa represents the electrode points around the chest wall just above the upper edge of the atria. The ordinates represent to the left the deviation of recorded to calculated potentials in mv and to the right the same as expressed in per cent of expectation (Bock and Baust 1954)

weakest in this series namely that the dipole concept is the only one with a sufficient foundation in physics We no longer regard the dipole of the heart as composed of two equal and spheric charges and we do not assume that the developing field is strictly identical with an ideal dipole field in the immediate neighborhood of the active fiber Nevertheless the dipole hypothesis is not only compatible with the membrane theory but is one of its obvious logical consequences (Schaefer 1941)

The German workers Ernsthausen and Kienle (1953) have seriously criticized the common vector concept They have stated that if the electric field surrounding a heart muscle fiber is calculated from intracellular recordings the field appears as in FIGURE 5 In this field pattern the isopotentials and the current lines have changed their respective positions According to Ernsthausen and Kienle these fields look like whirlfields and it was decided that potentials in these fields follow neither the cosine law nor the $1/r$ rule The summation of individual fiber potentials therefore cannot be calculated according to common vector analysis It should be noted however that there are some physical arguments that invalidate these critical remarks and cast doubt even on the correctness of FIGURE 5

No doubt the simultaneous presence of depolarization and repolarization events would force us theoretically to assume a quadrupole hypothesis in which the cosine as well as the $1/r^2$ law would be invalid Fortunately however the heart repolarizes at such a low rate that the depolarization vector does not interfere at all with the repolarization process Whatever special theory of the

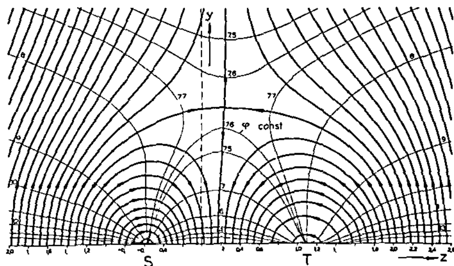


FIGURE 5 The static electric field of a single fiber producing an action potential according to the theory of Ernsthausen S is the center of depolarization and T is the center of repolarization The thick lines represent the current flow the thin lines are isopotentials The field is drawn only in the upper half of its cross section with the paper plane The fiber lies directly below the abscissa The figures on the abscissa and the ordinate give the distances and the potentials respectively in arbitrary units (Ernsthausen and Kienle 1953)

electric field one might postulate a vector concept will be acceptable as long as the resultant electrical source of the heart follows a cosine law and shows a diminution of its potentials according to $1/r^2$ As an example FIGURE 6 shows the accuracy with which the $1/r^2$ rule is obeyed by a frog heart immersed in a homogeneous conductor If this is the case the model of the vectorial concept leads to an excellent interpretation of the shape of the ECG thus furnishing us with at least some information of the way the excitation wave travels Since the known resulting vector is always defined by its unknown components and since consideration of the results alone does not permit an analysis of the unknown components the information yielded by the electric field of the heart is always a very limited one It consists more or less of conclusions as to the extent that the ECG in question is compatible with certain assumptions such as for example, the occurrence of a block of fibers or the diminution of the propagation velocity in all myocardial fibers Every ECG curve however has multiple possibilities of interpretation

The General Order of Excitation as Detected with Bipolar Surface Electrodes

Records obtained from the surface of the dog s heart with bipolar electrodes yield the following information (1) the propagation velocity (2) the local di

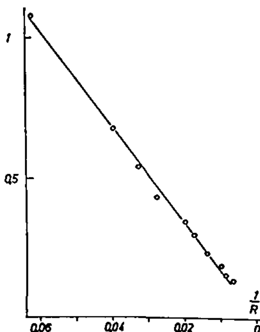


FIGURE 6 Relation between the local unipolar field potential and the distance R of the electrode from the center of the heart A frog heart fixed at a Straub cannula is mounted in the center of a cylinder containing Ringer s fluid The exploring electrode is moved along a radial line with a micromanipulator The ECG is recorded and the spike of R is measured The abscissa is $1/R^2$ (Dohrmann 1954)

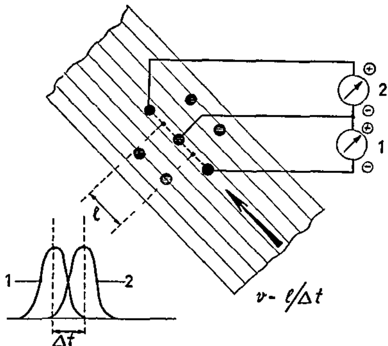


FIGURE 7a Schematic drawing of the compass electrode placed on the epicardial surface of a dog's heart Two amplifiers are connected in the manner indicated Various connections may be made by the use of a gang switch If the records are obtained from connections parallel to the muscle fibers the potentials and the peak to peak distance will reach a maximum as in the record below The excitation velocity v may be calculated from the symbols that are given

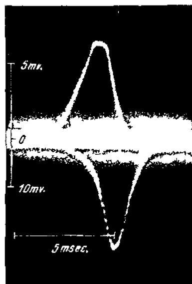


FIGURE 7b Original record made with the electrodes illustrated in FIGURE 7a For convenience the two action potentials are recorded with opposite polarity Cathode ray oscilloscope

rection of the excitation waves, and (3) the time sequence of their appearance. The direction may be determined easily by a device such as that shown in FIGURE 7. By switching the amplifiers through all possible combination positions for the electrodes on the diameter of the circle, we find at one of these positions a maximal potential difference and a maximal time delay between the two adjacent fiber portions below the pairs of electrodes. The direction of the excitation wave is identical with the axis of these electrodes. The propagation velocity may be calculated as usual from the observed time delay between the two action potentials. The instant of activation is measured by recording the time delay of the local excitatory process against a standard reference record.

The exploration of atrial activation in our laboratory (Brendel *et al.*, 1950) showed local latencies that are in agreement with the assumption that all waves are traveling on the shortest lines and with constant velocities from the sinus node to the periphery of the atria (FIGURE 8). The average velocity in the dog's atria measured 0.88 m./sec.

The behavior of the ventricles is far more complicated. Investigating the directions of excitation waves at the surface of the dog's heart, we noted that surface excitation seems to start in one narrow region of the anterior ventricular surface. We named this region the "source" (Quellpunkt) of excitation (Schaefer and Trautwein, 1949). This source apparently lies just above the deepest parts of the ventricular septum where the conduction system ramifies. This region is identical with the area in which the earliest arrival of excitation at the surface takes place (FIGURE 9). On the posterior surface of the heart, as shown in FIGURE 9a, we do not find a similar "source" (Trautwein, unpublished). We may conclude from this that the excitation process spreads along a system of lines represented in FIGURE 9b. The speed of the myocardial excitation measures approximately 1 m./sec. The relative times of activation of points at the surface, referred to a standard event of early cardiac activity, are represented in FIGURE 10. This illustration demonstrates that the "source" region of the heart is activated first and that the general order described for the spreading process holds also for time measurements. The early results of Harris (1941) are in complete agreement with our own (Schaefer and Trautwein, 1949). In spite of this agreement, however, these results require further explanation.

A Possible Mechanism of Activation of the Ventricular Wall

The velocity of the spreading process calculated from latencies such as those of FIGURE 10 would give values of 5 m./sec. and more. The propagation along the myocardial surface of the heart therefore cannot be explained in terms of the velocity of the excitation process in single myocardial fibers. Branches of the specific conduction system dip into various parts of the myocardium and this may excite small areas of the ventricular wall. As illustrated in FIGURE 11, the general philosophy concerning this activation process assumes that each terminal fiber of the specific conduction system eventually branches into numerous muscle fibers. Location of the borderline between the specific and nonspecific systems is a matter of choice. This ramification continues throughout

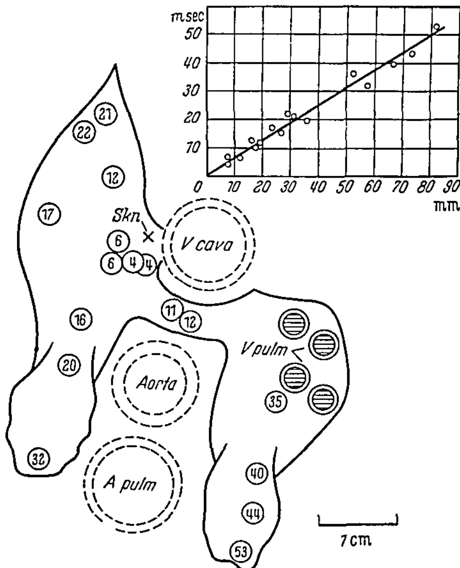


FIGURE 8 Atria and auricles of a dog s heart seen from the cranial site with the time given from the onset of *P* of a standard reference lead The time is in milliseconds The inset shows the times plotted against distances from the sinus region The excitation travels with a constant velocity of about 1 6 m per second in this experiment *Skn* indicates sinus node

the entire mass of the ventricular wall Each branching however supplies a system of more or less complete syncytial structure that builds up a wall of constant thickness and leads to innervation areas of a spindle structure Only with spindles of muscle fibers as given in FIGURE 11, are we able to cor



FIGURE 9 Map of the direction of surface excitation FIGURE 9a shows one experiment on the posterior surface of a dog s heart The results have been achieved with the technique shown in FIGURE 7 FIGURE 9b shows the anterior surface of the dog s heart The results of several experiments are indicated

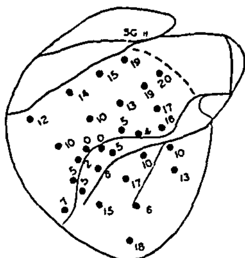


FIGURE 10 Relative arrival times in milliseconds of local action currents in a dog recorded with bipolar electrodes (Harris 1941) The source region of FIGURE 9a is the first to be activated

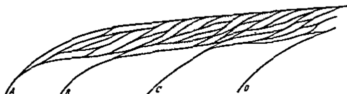


FIGURE 11 Possible mechanism of activation of the ventricular wall *A B C* and *D* are Purkinje fibers which branch into the myocardial system Each fiber activates a spindle like section of the ventricular wall The picture needs some corrections as given in FIGURE 17 to be a fairly good representation of real events

relate the system of ramification with the gross anatomy of the heart Of course the concept of 'ramification may be wrong and may have to be replaced by a concept of innervation' according to which branching fibers of the specific system extend into a homogeneous muscle strip as in the skeletal muscle Electrophysiological data seem to speak in favor of the assumptions represented in FIGURE 11

There is however one conclusion to be drawn from the concept represented in FIGURE 11 If we have an average velocity of the spreading process of 1 m/sec in the muscle fiber with about 5 m/sec activation velocity at larger areas of the ventricular surface there must be lines of inconstancy of the propagation Along these lines local action potentials picked up with suitable microelectrodes will reveal irregularities in the shapes of the potentials This is apparently the case FIGURE 12 shows such a picture with a marked diphasic behavior found in the vicinity of a surface point with very regular monophasic action potentials These lines of inconstancy should be identical with the boundaries of the spindles The investigation of this question however is not sufficiently advanced to yield a definite answer

Some Consequences Concerning the Interpretation of QRS

The pattern of activation found at the surface of the heart (FIGURE 9) is only an image of processes in the depth of the ventricular wall In spite of their symbolic nature these surface events indicate the general course of the excitation wave through ventricular musculature It is not likely that the main directions of excitation in the interior of the ventricular wall are completely different from those on the surface in so far as longitudinal (not circular) muscle layers are concerned This should mean that an excitation wave travels from a center in all directions building up an excitation front like that shown

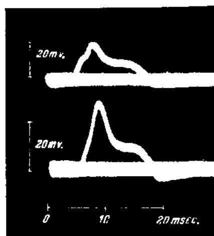


FIGURE 12 Record with a pair of electrodes with very small interelectrode distances put on the surface of a dog s heart as in FIGURE 7 The electrodes obviously lie just between two of the spindle areas of FIGURE 11

in FIGURE 13 If it is correct to assume that each fiber contributes its individual electric field to the field that produces the ECG tracings the intensity of this field is dominated by the amount of cancellation caused by these diverging excitation waves For instance in the neighborhood of the source two muscle fibers may branch out as shown in FIGURE 14 The fields of these fibers apparently cancel each other as soon as the electrodes are situated far enough from the cardiac surface to avoid any proximity potentials

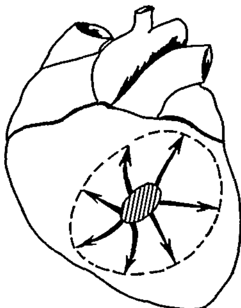


FIGURE 13 Schematic drawing of the excitation front found at the anterior surface during the R wave

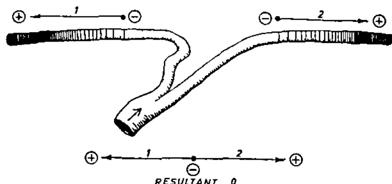


FIGURE 14 Model of a Purkinje fiber branching into two myocardial fibers the excitation waves of which run in a completely opposite direction The resultant potential field of both will be zero irrespective of any special assumptions concerning the properties of their individual electric field

It is possible to calculate the minimal amount of cancellation in the human heart on the basis of the following considerations we know that in extrasystolic beats the spreading process must be changed so that the excitation wave *travels more or less in one direction for example from an ectopic focus at the* apex toward the base A good picture of the uniformity of this spreading process is given by the local latencies and excitation fronts registered with bipolar electrodes in ectopic beats (Scher and Young 1955) By this method of propagation the cancellation factor becomes minimal (FIGURE 15) If we calculate the time potential areas of QRS in ectopic and in normal beats the quotient of their respective values defines the lower limit of cancellation The real amount of cancellation is in any case higher, because it is nearly impossible to avoid any cancellation completely The anatomical structure of the heart is such that fibers run in very different directions preventing propagation along strictly straight lines

My attempt (Schaefer 1952) to measure this quotient in extrasystolic beats of man gave an average value of 10 This means that at least 90 per cent of the potential produced by the ventricular fibers is cancelled by the divergence of excitation waves

If this value is taken as true we may conclude that blocking only 5 per cent *of the muscle mass and reversing the direction of the traveling excitation wave* in these fibers causes in the optimal recording leads, a change in the QRS area

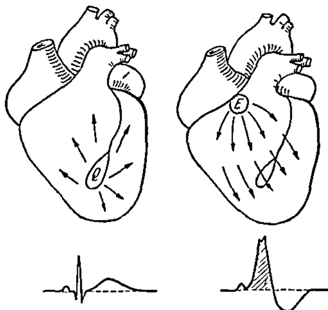


FIGURE 15 Model of the difference of the excitation process in normal and ventricular ectopic beats The extrasystolic beat has only a slight mutual cancellation of potentials and therefore a large time voltage area of QRS

that amounts to 100 per cent.* The QRS area is a very sensitive differential indicator of all changes in the direction of individual excitation waves. For instance, in the case of an inconstant Wolff-Parkinson-White (WPW) syndrome (FIGURE 16) the deformation of QRS can be attributed to the reversal of excitation waves in less than 9 per cent of the ventricular mass. These percentages are maximal values since every augmentation in the ratio of 10:1 (a minimal ratio) leads to the conclusion that a given percentage of reversed excitation waves has a comparatively greater effect on QRS.

The calculations represented in FIGURE 16 do not take into consideration the spatial orientation of the vectorial data. The calculation serves only as an example and may be easily extended to spatial magnitudes. No one will assume that calculations of this kind lead to accurate predictions as to the morphological basis of blocks or infarcts. What we have intended to discuss is merely the principle of such calculations. Better knowledge of the detailed way in which the ventricles are excited will enable us one day to express these calculations with more satisfactory accuracy.

Some Details of the Intramural Activation under the Aspect of Vector Analysis

Excellent work has been done in the United States in exploring ventricular activation. Multipolar needle electrodes have been inserted intramurally, and bipolar as well as unipolar records have been taken. A survey of investigations made in this way reveals a considerable variety of results. There is no doubt that extrasystoles elicited strictly below the exploring unipolar electrode are always of a pure QS type, that is, of a purely negative depolarization process. This is easily understandable since all excitation waves are traveling away from the point of origin of such ectopic beats. Therefore, the action potential must consist of a purely negative deflection. The same holds true for unipolar records with the electrode in the left part of the interventricular septum (Rothman *et al.*, 1954; Scher *et al.*, 1955). Apparently, the real source of the excitation front is to be found here. From this point the depolarization proceeds across the septum and the ventricular walls, reaching the surface first in the source region shown in FIGURE 10. We have learned from the very careful measurements of Scher and Young (1955) and Scher *et al.* (1953) that the depolarization front proceeds with very high speeds parallel to the ventricular surface and with rather low speeds across the wall. The process starts near the endocardial surface—how near is still a matter of controversy. Rothman *et al.* (1954) state that in the first one third to one half of the ventricular wall from the endocardium, the unipolar ECG is purely negative, and the bipolar leads of Durrer *et al.* (1954) show a reversal of the action potential if the leads are moved from the endocardial toward the epicardial surface.

This is due to the fact that the specific conduction system enters the ventricular wall at a certain depth and ramifies there. The endocardial layers may

* Five per cent of the fibers drop out in their normal direction and are therefore added to the opposite direction, which makes a difference altogether of 10 per cent. This, however, is the degree to which all electric potentials are canceled. This potential resulting from the cancellation process is of the same order of magnitude as the effect of blocking 5 per cent of the amount of muscle fibers.

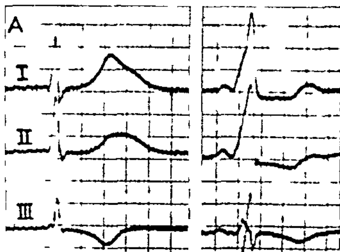


FIGURE 16a

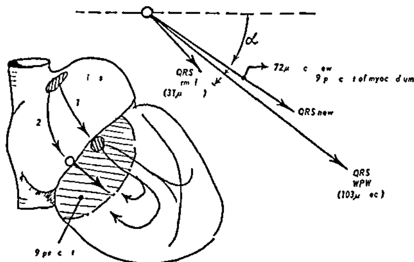


FIGURE 16b

FIGURES 16a AND 16b Attempt to calculate the minimal amount of muscle masses the action potentials of which must have been reversed by the abnormal excitation wave in a WPW syndrome The hypothetical calculation is made only for the frontal plane and needs a patial correction The whole procedure is only an example to demonstrate the general possibility of such calculations the correctness of which strongly depends on the validity of the vector theory FIGURE 16a shows the calculated ECG with normal and abnormal beats FIGURE 16b shows the vector analysis of the QRS waves both normal and abnormal giving the vector of a QRS area (new) produced by the inversion of excitation waves within the shadowed area Under the assumption that the cancellation factor is 1 10 as a minimal ratio the augmentation of QRS from 31 to 72 μvsec could be interpreted as the result of an inversion (as the result of pre excitation) in 9 per cent of the total ventricular mass This inverted wave starts from the point activated by the atrial bundle (2) The arrow in the shaded area indicates the average direction of fibers in the inverted area

accordingly be activated inward Depending on the depth of this branching point the results of unipolar leads are quite different Bipolar as well as unipolar records from endocardial or intramural points near this branching area are very difficult to explain in full detail since even the polarity of deflection depends completely on the random distribution of fibers and their respective potential differences between the electrodes Conclusions drawn by workers seem uncertain in the light of vector analysis

The absence of any intrinsic deflection in endocardial leads as well as in cavity leads only points to the fact that the amount of equivalent fiber masses whose waves run away from the electrodes far exceeds the equivalent amount of fibers with approaching waves Since in the interior of a closed sphere of the ventricular cavity two layers of muscle masses are found one activated from the branching point to the interior the other from the branching point to the exterior of the ventricular wall the resulting potential depends only on the respective masses of these two parts of the wall Since the inner part of the wall extending to the branching plane of the specific system seems always to be smaller than the outer part the prevailing negativity in all endocardial and cavital leads is easily explained It is necessary however briefly to discuss what the term intrinsic deflection really means and why this deflection is absent in endocardial leads

A strong intrinsic deflection that is a downstroke of more than 10 mv in amplitude and of a very high slope (about 10 mv /1 msec) occurs only if a solid mass of muscle is activated nearly synchronously in all fibers running more or less uniformly toward the electrode The potential would reach the maximal value of about 100 mv if viewed from the exploring electrode all activated cross sections of myocardial fibers would add to the solid angle of 360° Even if there is a uniform mass of active fibers running in a uniform direction and excited at the same time a surface electrode never could exceed the potential difference of about 50 mv since the olid angle never exceeds 180 Values of about 40 mv as a matter of fact are the upper limits of the peak potentials in unipolar records

If an intrinsic deflection is lacking as in the case in endocardial leads the conclusion would be merely that no considerable mass of active muscle fibers forming an activation front of a sufficient by large solid angle is present As remote muscle masses (FIGURE 3) contribute their part to the unipolar potential the effect of receding excitation waves overwhelms every intrinsic effect and the result is a pure negativity in spite of small muscle masses that carry excitation waves running toward the electrode The effect of unipolar leads is the integral of all events occurring in the surrounding space and appearing under sufficiently large solid angles to contribute to the electric field of the exploring electrode

The General Order of the Repolari ation Process

In contrast to the fairly well known processes that form the QRS complex we are in complete darkness about all events governing the production of the T wave I might well omit this entire problem here as it constitutes the sub-

ject of another part of this monograph namely of the ventricular gradient The fact however that the gradient is the only and rather inadequate criterion of differences between the orders of depolarization and repolarization makes it inevitably necessary to present at least a general idea of what the ventricular gradient actually is As Wilson *et al* (1934) and Ashman and Byer (1943) have pointed out the areas of QRS and T should sum up to zero if the polarity of all parts of QRST is taken into consideration and if one assumes that all parts of the heart repolarize with a similar shape of the action potential T points mostly in the same direction as the main deflection of QRS however and therefore the sum of QRST areas calculated as a vector in the frontal plane is 50 µvsec on the average

This deviation of a normal human heart from the expected "normal electrophysiological behavior requires an interpretation in physical terms Unfortunately the interpretation of the T wave is fully dependent on that of the ventricular gradient This is because a negative (discordant) T of the same area as QRS would indicate only that repolarization follows the same order as the preceding depolarization

The difficulties of the problem in question derive from the following situation the events in the innumerable heart fibers are more or less asynchronous Nevertheless they complement each other and add their potentials to a resulting field Due to the asynchronism of the fibers only the area of QRS is comparable with the area of T since the repolarization (T) is of very much longer duration than R and the addition of the individual fields of all fibers during T is less dependent on the slight differences in latency The absolute amplitudes of T compared with QRS are therefore without a precise meaning* If peculiarities of the repolarization process are to be observed the only method of value is the integration of QRS and T areas and their comparison *Whether this area the ventricular gradient has a physical meaning or not is completely irrelevant* It is the only way to measure those changes of T that are independent of changes of QRS

This latter fact involves a rather disturbing consequence the deviation of T from the state of expected physiological normality can be judged only by this area technique but the areas of QRS and T calculated as vectors no matter whether spatial or only in the frontal plane have no definite physical or geometrical meaning The real event of myocardial excitation and recovery can be recorded only as a time voltage area of the resulting vector This vector has been registered by several authors (Hollmann 1939 Mann 1938 Sayers 1955) by some simple device such as monocardiogram or absolute ECG The spatial construction of QRS or T areas however does not lead to the area that the resultant vector would give in a potential time record This can easily be shown either by analysis or by a simple test Thus the spatial construction of all areas of the ECG leads to arbitrary values without any definite meaning

In only one case can physical significance be attributed to such area vectors namely when the resultant of the inhomogeneous repolarization shows a uni

* It is not permissible to take the QRS loop as identical with the loop of G if T is zero has been done by Burch *et al* (1954)

form direction during the whole QT period In this case when rotations of the resultant vector of all potential forces of the ventricular gradient are absent the gradient may be regarded as the time potential area of a resultant vector recorded in its momentary strength during the course of the QT period It is apparently possible to assume that larger rotations of the gradient vector are actually missed as the loop of T runs nearly in a constant direction It remains uncertain however whether the gradient may be attributed solely to inhomogeneities in the repolarization slope of the various parts of the ventricle

We may omit all objections to the concept of the ventricular gradient Simonson *et al* (1954) have made an excellent list of critical remarks the most important and general points of which are that the gradient may be due to an interaction of fibers with their inhomogeneous impedance and polarization or it may be caused by changes in the geometry of the heart (rotation contraction) or by the inhomogeneous properties of the fibers (tapering changes in shape or excitation velocity in monophasic potential) Only the last argument has been discussed in the literature thus far Its accuracy is illustrated in FIGURE 17 which shows the differences between monophasic action potentials at various points of the heart surface (Schaefer and Scholmerich 1943) The question however would be What kind of mechanism leads to such differences?

There are some facts that probably contribute to the analysis of the nature of ventricular gradients (1) the gradient does not change in an isolated dog s heart with the filling pressures diameters and diastolic volumes (Bock *et al* 1954) (2) in the isolated myocardial fiber there is no difference in the form of action potentials if the fiber is stretched (Dudel and Trautwein 1954), for both facts show that purely mechanical factors cannot be claimed as the only source of the gradient in spite of some impressive clinical data (Schaefer 1951) and (3) the spatial gradient has a strong correlation to the magnitude of the spatial QRS area (Simonson *et al* 1954) FIGURE 18 indicates these conditions for the frontal plane gradient In our own experience the angle of the gradient has a very close correlation to the angle of the QRS area (FIGURE 19) This suggests that the gradient probably has something to do with the spatial distribution of the myocardial fibers Gradient and QRS likewise depend on the same object namely the anatomical structure of the heart

There is little hope of gaining a perfect and lasting theory of the order of repolarization processes with our present knowledge The best hypothesis

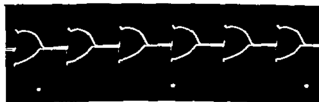


FIGURE 17 Monophasic action potentials from the basis (upper curve) and the apex (lower curve) of a cat s heart. Suction electrode with narrow distance (about 1 mm) to the different electrode Time marks 1 second The apex potential is recorded top down (Schaefer *et al* 1943)

seems to be the assumption that there are several factors that determine the magnitude and angle of T and of the gradient One could assume that an indirect influence is exerted by the mechanics of the heart in improving or depressing the blood supply of the various layers of the ventricular wall The

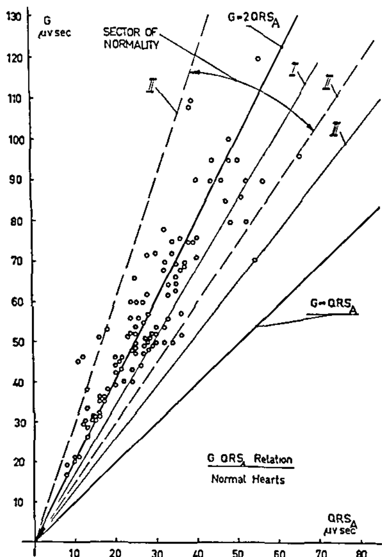


FIGURE 18 Correlation between the QRS area and the ventricular gradient in normal hearts with all values taken from the frontal plane projection Nearly all values (7 exceptions) are lying in a sector of normality around a line giving the relation $G = 2$ QRS Lines II are the borderlines of the sector of normality giving the relation $G = 3$ QRS and $G = 1.5$ QRS Line I separates the normal from the failing hearts Line III gives the lowest limit of normal G in relation to QRS area ($G = 1.3$ QRS area) (Courtesy of W Gärtner)

inner layers are always less perfused than the outer surface, due to increasing intramural pressures that oppose the capillary blood pressure. Indeed, the blood flow strongly influences the shape of monophasic action potentials (Trautwein *et al.* 1954), but this effect goes in the wrong direction. Since the hypoxic fiber repolarizes earlier, the duration of the excitatory phase should be earlier, and the endocardial layers should be relatively positive to the outside. The hypoxia concept, moreover, is invalidated by the fact that a major diminution of blood pressure in hypertensive patients has not (Pipberger *et al.* 1955) or has only slightly (Brumlik and Kossmann 1952) altered the magnitude and direction of T or of the ventricular gradient. Only the pulse pressure has shown a positive correlation with the magnitude of the gradient (Friese *et al.* 1955), but this only indicates a correlation between the gradient and the stroke volume.

The extent to which the temperature gradient, due to the metabolic heat of the heart muscle, adds to the inhomogeneities of repolarization is still not known with certainty. The endocardial layers, cooled by the blood stream, should be brought to a longer excitation as compared with the rest of the myocardial wall. The temperature gradients observed (Dohrmann and Engelking 1956) indicate strong effects. Our own experiments during recent months, however, seem to demonstrate that the temperature is not the only cause of the ventricular gradient.

If we try to give a preliminary hypothesis of the general order of repolarization in the heart, we may use the following model: the inhomogeneous repolari-

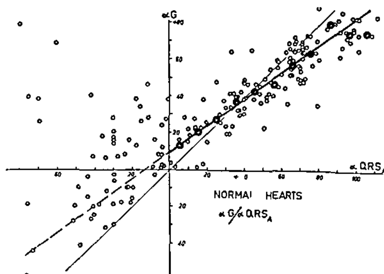


FIGURE 19. Correlation between angle α of the QRS area and α of the ventricular gradient taken for the frontal plane. The large dots are the averages. The thick line represents the equation $\alpha G = 0.72\ \alpha QRS + 10$ and applies to normal subjects and to patients without clinical signs of failure. In the left ventricular strain (αQRS negative) the correlation disappears almost completely. (Courtesy of W. Gärtner.)

zation or whatever else might produce the gradient depends on at least two different mechanisms One of them is closely correlated to the QRS area It might be an inhomogeneous repolarization due to fiber tapering or to any other process developing automatically with the progress of the excitation wave in the ventricular wall The underlying basic event may be a shortening of the monophasic action potential The smaller the myocardial fiber becomes the shorter the duration of the plateau will be This of course is for the moment a completely hypothetical assumption We know only that there are consid

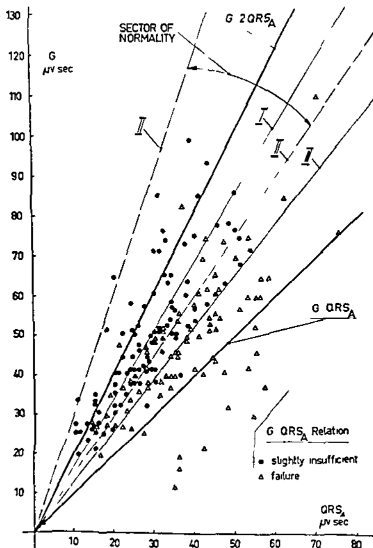


FIGURE 20A

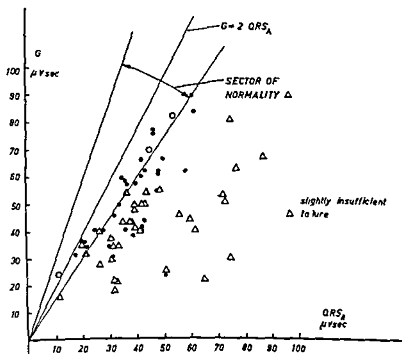


FIGURE 20b

FIGURES 20a AND 20b Correlation between the QRS area and the ventricular gradient in the frontal plane in clinically abnormal hearts (lines as in FIGURE 18) Slightly insufficient means that of a series of clin cal tests no more than two were borderline Failing hearts showed at least one abnormal result FIGURE 20a shows patients without infarcts blocks valvular diseases or hypertension FIGURE 20b shows patients with hypertension only (Courtesy of W Gärtner)

erable differences in the shape of the monophasic action potentials (Coraboeuf *et al* 1953)

A second process may consist of differences of unknown character between the inner and outer layers of the ventricular wall varying with temperature and with mechanical or other unknown factors Both processes together add up to a magnitude of approximately 2 × QRS area (FIGURE 18) The rotation of QRS interferes with this second and relatively independent process On the average the angle of the gradient thus depends on the angle of QRS according to the equation (FIGURE 19)

$$\alpha G = 0\,72 \times (\alpha \mathrm{QRS}_A) + 10$$

Ashman *et al* (1943) have argued that the spatial angle between QRS_A and G and a rotation about the anatomical heart axis may produce this correlation The evidence of these authors is good but not entirely conclusive

The gradient concept involves a second problem namely the clinical applicability There have been many attempts to show that the clinical value of

the gradient is small or even absent (Koehler and Spang, 1953, Meyer and Herr 1951 Unghvary and Farkas 1954, Welsch and Wieland 1953) Simonson *et al* (1954) in particular have come to the conclusion that nearly all gradient values usually regarded as pathological are within normal limits This may be true but it does not touch the theory of the gradient The gradient is the only correct entity that indicates changes of T that are independent of QRS Thus only the gradient provides us with more information than we may obtain by an analysis of QRS If the gradient proves to be worthless in special cases the same should be true for T If, therefore even in severely pathological hearts the gradient lies within normal limits this implies the necessity of a correction either of the term normal or of the current interpretation of T As a matter of fact the gradient may show nearly all values even in normal hearts (FIGURE 18) This is due to the fact that G lies between the values of 3 × QRS and 1 5 × QRS If G is compared with QRS_A however the limits of normality seem to be very narrow and most of our own examples considered as abnormal are clearly pathological also in their gradient values whereas Simonson *et al* (1954) considered only the absolute value of G irrespective of the QRS area (FIGURE 20) No significant difference is noticeable between normal and failing hearts concerning the angle of G and its relation to the angle of QRS

References

ASHMAN R & E BYER 1943 Am Heart J 25 16
ASHMAN R M GARDBERG & E BYER 1943 Am Heart J 26 473
BAUST W K D BOCK & R DOHRMANN 1954 Cardiologia 25 118
BOCK K D & W BAUST 1954 Z Kreislaufforsch 43 624
BOCK K D R DOHRMANN & W TRAUTWEIN 1954 Cardiologia 25 363
BRENDEL W W RAULE & W TRAUTWEIN 1950 Pflügers Arch ges Physiol 253 106
BRUMLIK J & C E KOSSMANN 1952 Circulation 5 712
BURCH G E J A ABILDSKOV & J A CRONVICH 1954 Circulation 9 267
CORABOEUF E R DISTEL & J BOISTEL 1953 Compt rend soc biol 147 1757
DOHRMANN R 1954 Z Kreislaufforsch 43 699
DOHRMANN R & R ENGELKING 1956 Z Kreislaufforsch 45 651
DUCHOSAL P & R SULZER 1949 La Vectorcardiographie Karger Basel Switzerland & New York N Y
DUDEL, J & W TRAUTWEIN 1954 Cardiologia 25 344
DURRER D & L H VAN DER TWEEL 1954 Am Heart J 47 192
DURRER D L H VAN DER TWEEL & J R BLICKMAN 1954 Am Heart J 48 13
ERNSTHAUSEN W & F KIENLE 1953 Das elektrische Herzbild Verlag H Rinn Munich Germany
FRANK F 1955 Am Heart J 49 670
FRIESE G K MECHELKE & W ULMER 1955 Z Kreislaufforsch 44 517
GÖPFERT H 1951 *In* H SCHAEFER. Das Elektrokardiogramm Springer Verlag Berlin Gottingen & Heidelberg Germany
GROEDEL F M & P R BORCHARDT 1948 Direct electrocardiography of the human heart Brooklyn Med Press New York N Y
HARRIS A S 1941 Am J Physiol 134 319
HARTMANN J P VEYRAT O A M WYSS & P W DUCHOSAL 1955 Cardiologia 27 129
HOLLMANN W 1939 Verhandl deut ges Kreislaufforsch 12 111
JOUVE A M ALBOUY I VELASQUE G BERGER & P NICOLAI 1953 Arch maladies coeur et vai eaux 46 508
KIENLE F 1955 Grundzüge der Funktions Elektrokardiographie Verlag Braun Karlsruhe Germany
KOEHLER F & K SPANG 1953 Arch Kreislaufforsch 20 138

LEVINE R B O H SCHMITT & F SIMONSON 1953 Am Heart J 45 500
LEWIS J & M S ROTHSCHILD 1915 Phil Trans Roy Soc B206 181
MANN H 1938 Am Heart J 15 681
MEYER P & R HERR 1951 Arch maladies coeur et vaisseaux 44 119
MEYER P J F MERLEN & R KLEIN 1955 Arch maladies coeur et vaisseaux 48 959
LIPBERGER H R KALIN & P H ROSSIER 1955 Cardiologia 27 166
ROTHMAN S E GERLACH M PRINZMETAL L KAKITA & J L BORDUAS 1954 Am J Physiol 179 557
SAYERS B McA 1955 Am Heart J 49 336
SCHAEFER H 1941 Pflügers Arch ges Physiol 245 72
SCHAEFER H 1950 Verhandl 18 int Kongr Physiologie Zürich 429
SCHAEFER H 1951 Das Elektrokardiogramm Verlag Springer Berlin Gottingen & Heidelberg Germany
SCHAEFER H 1952 Pflügers Arch ges Physiol 255 251
SCHAEFER H A PENA & I SCHOLMERICH 1943 Pflugers Arch ges Physiol 246 728
SCHAEFER H & W TRAUTWEIN 1949 Pflügers Arch ges Physiol 251 417
SCHAEFER H & W TRAUTWEIN 1951 Pflügers Arch ges Physiol 253 152
SCHER A M & A C YOUNG 1955 Circulation Research 3 535
SCHER A M A C YOUNG A L MALMGREN & R V ERICKSON 1955 Circulation Research 3 56
SCHER A M A C YOUNG A L MALMGREN & R R PATON 1953 Circulation Research 1 539
SCHMITT O H R B LEVINE & E SIMONSON 1953 Am Heart J 45 416
SIMONSON E O H SCHMITT J DAHL D FRY & E E BAKKEN 1954 Am Heart J 47 122
SIMONSON E O H SCHMITT R B LEVINE & J DAHL 1953 Am Heart J 45 655
SODI PALLARES D E BARBATO & A DELMAR 1950 Am Heart J 39 387
SODI PALLARES D A BISTENI G A MEDRANO & F CISNEROS 1955 Am Heart J 49 587
TRAUTWEIN W U GOTTSTEIN & J DUDEL 1954 Pflugers Arch ges Physiol 260 40
UNGHVARY L & F FARKAS 1954 Z Kreislaufforsch 43 468
VEYRAT R 1953 Helv phys acta 11 395
WELSCH A & H WIELAND 1953 Z Kreislaufforsch 42 262
WILSON F N A G MACLEOD P S BARKER & F D JOHNSTON 1934 Am Heart J 10 46
WILSON F N F F ROSENBAUM & F D JOHNSTON 1947 Advances in Internal Med 2 1

the gradient is small or even absent (Koehler and Spang 1953 Meyer and Herr 1951 Unghvary and Farkas 1954 Welsch and Wieland, 1953) Simonson *et al* (1954) in particular have come to the conclusion that nearly all gradient values usually regarded as pathological are within normal limits This may be true but it does not touch the theory of the gradient The gradient is the only correct entity that indicates changes of T that are independent of QRS Thus only the gradient provides us with more information than we may obtain by an analysis of QRS If the gradient proves to be worthless in special cases the same should be true for T If therefore even in severely pathological hearts the gradient lies within normal limits this implies the necessity of a correction either of the term normal ' or of the current interpretation of T As a matter of fact the gradient may show nearly all values even in normal hearts (FIGURE 18) This is due to the fact that *G* lies between the values of 3 × QRS and 1 5 × QRS If *G* is compared with QRS_A however, the limits of normality seem to be very narrow and most of our own examples considered as abnormal are clearly pathological also in their gradient values whereas Simonson *et al* (1954) considered only the absolute value of *G* irrespective of the QRS area (FIGURE 20) No significant difference is noticeable between normal and failing hearts concerning the angle of *G* and its relation to the angle of QRS

References

ASHMAN R & E BYER 1943 Am Heart J **25** 16
ASHMAN R M GARDBERG & E BYER 1943 Am Heart J **26** 473
BAUST W K D BOCK & R DOHRMANN 1954 Cardiologia **25** 118
BOCK K D & W BAUST 1954 Z Kreislaufforsch **43** 624
BOCK K D R DOHRMANN & W TRAUTWEIN 1954 Cardiologia **25** 363
BRENDEL W W RAULE & W TRAUTWEIN 1950 Pflügers Arch ges Physiol **253** 106
BRUMLIK J & C E KOSSMANN 1952 Circulation **5** 712
BURCH G E J A ABILDSKOV & J A CRONVICH 1954 Circulation **9** 267
CORABOEUF E R DISTEL & J BOISTEL 1953 Compt rend soc biol **147** 1757
DOHRMANN R 1954 Z Kreislaufforsch **43** 699
DOHRMANN R & R ENGELKING 1956 Z Kreislaufforsch **45** 651
DUCHOSAL P & R SULZER 1949 La Vectorcardiographie Karger Basel Switzerland & New York N Y
DUDEL J & W TRAUTWEIN 1954 Cardiologia **25** 344
DURRER D & L H VAN DER TWEEL 1954 Am Heart J **47** 192
DURRER D L H VAN DER TWEEL & J R BLICKMAN 1954 Am Heart J **48** 13
ERNSTHAUSEN W & F KIENLE 1953 Das elektrische Herzbild Verlag H Rinn München Germany
FRANK E 1955 Am Heart J **49** 670
FRIESE G K MECHELKE & W ULMER 1955 Z Kreislaufforsch **44** 517
GÖPFERT H 1951 *In* H SCHAEFER Das Elektrokardiogramm Springer Verlag Berlin Gottingen & Heidelberg Germany
GROEDEL F M & P R BORCHARDT 1948 Direct electrocardiography of the human heart Brooklyn Med Press New York N Y
HARRIS A S 1941 Am J Physiol **134** 319
HARTMANN J R VEYRAT O A M WYSS & P W DUCHOSAL 1955 Cardiologia **27** 129
HOLLMANN W 1939 Verhandl deut ges Kreislaufforsch **12** 111
JOUVE A M ALBOUY P VELASQUE G BERGER & P NICOLAI 1953 Arch maladies coeur et vaisseaux **46** 508
KIENLE F 1955 Grundzuge der Funktions Elektrokardiographie Verlag Braun Karlsruhe Germany
KOEHLER I & K SPANG 1953 Arch Kreislaufforsch **20** 138

termining how these affect body surface recording points The second constant K_2, is so determined

$$E_p = \Omega\Phi K_1 K_2$$

$$= \frac{V}{4\pi}\frac{A}{R^2} K_1 K_2$$

Work in our laboratory has concerned the pathway of depolarization[3, 4, 5] and the determination of the variable volume conductor constant, K_2[6] The first of these will be discussed

Depolarization of the Ventricles

The multipolar electrode used in these studies (FIGURE 1) consists of 15 fine insulated wires with bare tips staggered at 1 or 0 5 mm intervals Potential changes at the recording tips are amplified and displayed on a 16 channel oscilloscope (FIGURE 2) Since the electrodes are small (maximum diameter 0 3 mm) and flexible they cause little damage and many of them can be in

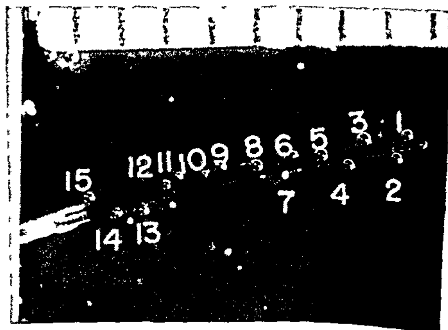


FIGURE 1 Multipolar electrode of the type used to trace ventricular depolarization The 15 terminals are spaced ½ mm apart The maximum diameter of the asse[illegible] is ¼ m[illegible] A bubble has been placed at each terminal by the passage of current in a water [illegible] [illegible] is in *millimeters*

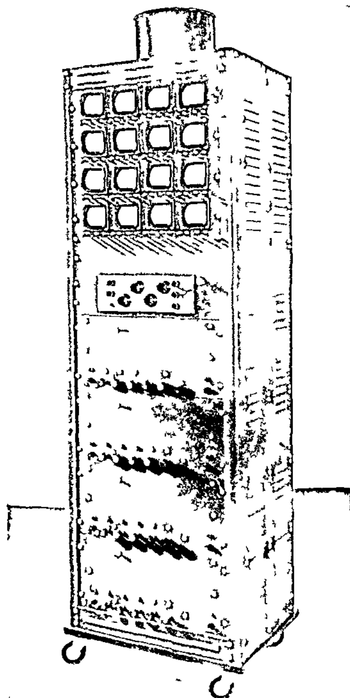


FIGURE 2 Sixteen channel oscilloscope used to display and photograph potentials from the multipolar electrodes. It consists of 4 banks of 4 tubes each, each bank with its own power supply. The sweep generator and triggering units are in the center



FIGURE 3 Stroboscopic flash photograph of a beating dog heart Eight electrodes are arranged in a coronal section in the ventricles The stripes on the electrode shafts are behind the recording tips The electrode in the center of the heart serves as a time reference

serted either successively or at the same time into each heart studied FIGURE 3 shows a beating heart containing 8 electrodes inserted coronally

Potentials from the electrode are recorded in two fashions A unipolar record shows the potential difference between each terminal and the left fore arm A bipolar record measures differences between adjacent terminals A fixed time reference potential is continually recorded as is a lead II electro cardiogram Simultaneous time marks are fed to all channels from a single oscillator In a unipolar record approaching activity is signaled by a positive deflection receding activity by a negative deflection Depolarization at the recording tip likewise gives a negative deflection usually with a much faster rate of change than that produced by receding activity Unipolar records represent a summation of nearby and distant activity They cannot be used to time local activity or to measure velocities

A unipolar record taken across the mid left lateral ventricular wall of a rhesus monkey is shown in FIGURE 4A The first 3 terminals were in the cavity and the potentials recorded on these consisted of a slow negative wave lasting about 30 msec Activity receded from these left cavity points during most of QRS Channel 4 which recorded from muscle bordering the endocardium showed a negative deflection that was faster in onset and of shorter duration than the cavity record The elevation of the base line indicated persistence of some injury at this terminal Channels 5 to 8 displayed similar wave shapes

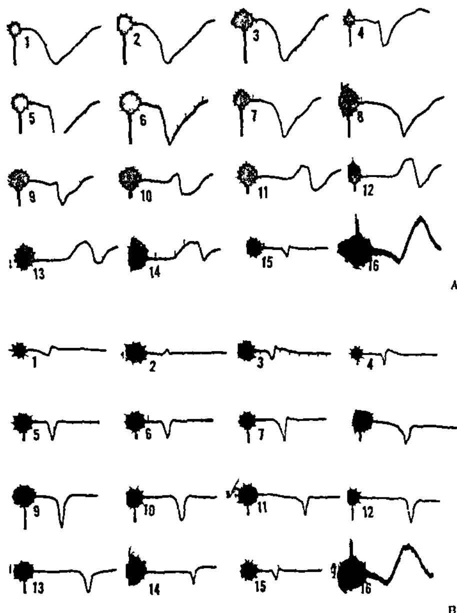


FIGURE 4 Potentials recorded across the mid lateral left ventricular wall of the rhesus monkey. A represents the unipolar potentials. B represents the bipolar potentials. Terminals 1, 2 and 3 of the unipolar record show the characteristic central left cavity records. The 15th terminal, from which no unipolar record is taken, was at the epicardial surface. Bipolar channel 1 records the potential difference between unipolar records 1 and 2, and bipolar channel 2 records the potential difference between 2 and 3, etc. Channel 15 records *the fixed time reference potential and channel 16 records the lead II QRS*

although some negative (receding) activity preceding local depolarization appeared on channels 7 and 8 On channels 9 to 14 there was some receding activity but the records show a positive deflection preceding local depolarization, progressively greater as we approach the epicardium When this record was photographed terminal 15 from which no unipolar record was taken was at the epicardial surface

Bipolar records from the same electrode are shown in FIGURE 4B Channel 1 of the bipolar record shows the potential difference between unipolars 1 and 2 etc By convention downward bipolar deflections indicate activity moving from inside outward in the heart The time of depolarization between the two terminals can be determined by measuring the positive or negative maxima of the bipolar records and comparing these with the fixed time reference The succession of downward bipolar potentials indicates qualitatively and the measurements to the negative peaks quantitatively that the depolarizing wave moves from endocardium to epicardium The rate of passage along the electrode is about 0 5 m /sec but exact velocity can be calculated only between successive portions of the wave front in a three-dimensional plot of excitation Any electrode not parallel to the direction of advance will indicate a higher than actual velocity

The major intention of this report is to present a picture of total ventricular activity However the excitation pattern in portions of the myocardium during premature ventricular systoles and after experimental bundle branch block will be briefly mentioned

The basic principles of excitation can be studied in simple cross sections of the heart and more successfully in blocks of tissue A cross section containing 6 electrodes is shown in FIGURE 5 Time of activity in milliseconds before or after the time reference is noted opposite most of the terminals Along electrode 39 in the right wall activity moved from inside outward as it did for 5 mm or more near the epicardium along the electrodes in the left wall Electrodes 45 and 46 which penetrated the anterior left papillary muscle showed complicated patterns of excitation near the endocardium Along electrode 46 the direction of activation reversed twice Electrode 43 at the apex penetrated the endocardium 3 times which also led to a complicated pattern The septal electrodes 41 and 42 showed double envelopment of the septum from both endocardial surfaces As can be seen the over all movement is from endocardium to epicardium Normally much of the endocardium is excited quite rapidly by the rapidly conducting Purkinje system which consists of elements conducting at about 1 m /sec The apparent velocity of Purkinje conduction often exceeds this value because the fibers branch extensively In the peripheral and particularly in the basal parts of the endocardium these fibers may be relatively unbranched and/or sparse Conduction through muscle is at about $\frac{1}{3}$ m /sec Occasionally the direction of movement in the walls reverses and at times there is extremely rapid excitation over a few millimeters from the endocardium[7] Reversal is particularly present under papillary muscles as is simultaneous excitation under deeper trabeculations (FIGURE 5) We do not consider these to be general phenomena nor do we

think that simultaneous activation indicates a universal intramural penetration of the rapidly conducting Purkinje fibers These phenomena are not found in the right ventricle nor in the septum Moreover rapid excitation of part of the wall thickness is not confined to the regions near the endocardium and is often found to result from excitation by two waves approaching each other from different directions

The principles stated above can be tested by starting premature systoles at known positions and plotting the resultant spread of activity The findings support the idea that elements of the Purkinje network conduct at 1 m /sec since this is the fastest endocardial rate found during extrasystoles and since the Purkinje fibers evidently are excited in extrasystoles Spread through the wall as in the normal systole is at about 1/3 m /sec

Excitation in experimental bundle branch block has been extensively studied by R V Erickson and his co workers[8] Their findings support the general views stated above In right bundle branch block the prolonged ventricular complex has two causes (1) increased time required for septal activation the normal double septal envelopment being replaced by one way spread from the unblocked side and (2) increased time required to excite the wall In bundle

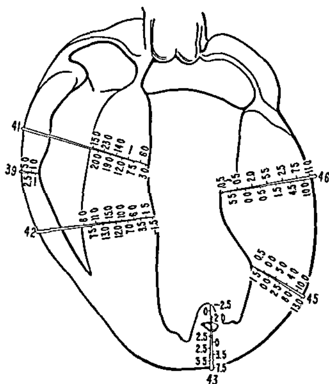


FIGURE 5 Time of activity in milliseconds before or after the time reference potential in a coronal section of the dog heart

branch block the area of initial mural endocardial activity on the blocked side is determined by septal activation and the area initially activated is small compared to that initially depolarized by the branched Purkinje network in normal depolarization Activation of the mural endocardium on the blocked side may require twice as much time as is needed for normal activation This finding is in accord with the view of Smith and his co workers [9]

FIGURE 6 is a diagram of total ventricular activation The lead II electro cardiogram reproduced from the oscilloscope records has been divided into 5 msec intervals Tissue activated during each interval is shaded in a different fashion The heart is shown divided into 4 sections by planes roughly parallel to the apex and the basal plane of each section is illustrated The 4 planes contain 17 electrode tracks indicated by solid lines Over 60 insertions were made in this heart from which more than 900 records were taken Much information was obtained from electrodes that lay outside the 4 planes shown

The earliest recorded activity indicated by the cross hatched regions bor dered the left cavity on the septal surface in the central sections Activity extended between these 2 sections and beyond them both apically and basally This region is near the termination of the left bundle There may have been other activity during this early period but it was not recorded This small mass of tissue is the only tissue that is silent at normal QRS amplification

Within the next 5 msec (region of large dots) activity had extended on the left to include muscle near the endocardium in all sections A complete ring of depolarized muscle surrounded the left cavity in the second section and there were extensive but incomplete rings around the cavity in the apical and third sections Activity also extended slightly into the posterior basal section At this time the area of depolarized myocardium on the left resembled an irregular conical section truncated both apically and basally On the right activity was confined to the third and basal sections This activity spread from the terminations of the right bundle near the anterior right papillary muscle The activated depolarized area had the shape of an irregular folded sheet of activated muscle around the anterior right cavity

Areas excited during the next 5 msec period are designated by the vertical lines It should be noted that this period brings us one quarter of the way through QRS in the dog The time required for depolarization in the dog is less than half that required in the human and a conversion factor of 2 or 2 5 is necessary During this period there was much extension of the depolarized tissue on both sides On the left a complete cone of active tissue extended through all sections around the cavity (except of course in the fibrous region between cavity and aorta in the basal section) On the right the cone was in complete although there was a complete ring in the apical section where the right cavity is almost indistinguishable Two very important changes took place during this period The activity around each cavity joined in the sep tum and endocardial breakthrough occurred on the right

The next 5 msec period (contour lines) brings us almost halfway through QRS During this period there was further activation toward the epicardium The tips of the papillary muscles on the left were also activated In all three

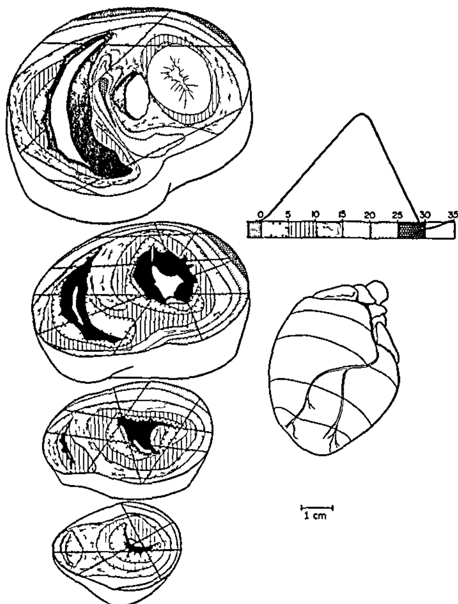


FIGURE 6 A plot of total ventricular activation Seventeen electrode tracks are shown in 4 cross sections of the heart The time of activity in milliseconds before or after the time reference was noted at each terminal of the electrodes (electrodes were inserted across the heart and gradually withdrawn to prevent overlap between successive positions of each electrode) A single correction was applied to correct all times to the beginning of the lead II QRS Lines were then drawn to connect the points activated at 5 msec intervals Tissue activated within each 5 msec interval is shaded in the same manner in all sections

apical sections the active regions around the right and left cavities were joined in the septum Endocardial breakthrough on the right was greatly increased in the three apical sections and some breakthrough occurred on the anterior left and lateral right in the basal section In the basal region an irregular trench of resting tissue on the anterior right extended into the septum

The next 5 msec period (areas of small dots) saw further epicardial movement of the activating wave with extension of epicardial breakthrough In the following 5 msec (diagonal lines) excitation in the two apical sections was completed and only a small slice of posterior tissue in the wall in the two basal sections remained to be excited There was also a central septal region that was excited during the last 5 msec

No records of activity after 30 msec were obtained in these sections Other records indicate that the latest regions depolarized are in the basal septum This finding corroborates the early reports by Burchell[10] and by Sodi Pallares[11] and their co workers

Genesis of QRS

The earliest activity is on the left of the septum at the terminations of the left bundle and is predominantly a movement to the right in the septum This may give a negative (Q) deflection in lead II although no such deflection appears in FIGURE 6 From this region and from the termination of the right bundle activity rapidly involves a large part of the endocardium and commences to move epicardially in the wall and toward the center of the septum from both sides We can think of this activity as leading to numerous vectors whose over all orientation is toward the apex This apically oriented vector is in part the sum of activity moving roughly perpendicular to the walls on the right and left As the posterior right ventricle becomes activated and as epicardial breakthrough becomes more prominent on the anterior right the vector will shift to the left and posteriorly By the end of 20 msec, halfway through QRS the predominance of leftward and posteriorly directed activity is established

As breakthrough on the left and posterior becomes more extensive apically the vector swings perpendicular to lead II and finally toward the base The final negative deflection in this lead undoubtedly reflects activity in the basal walls and more important activity pointing toward the auricles in the central septum The three simplest vectors derived from the above are right to left base to apex and apex to base The second is of course predominant and the transitions among the three are quite smooth

References

1 WEIDMANN S 1956 Elektrophysiologie der Herzmuskelfaser Hans Huber Bern Switzerland
2 WILSON F N A G MACLEOD & P S BARKER 1933 The distribution of action currents produced by heart muscle and other excitable tissues immersed in extensive conducting media J Gen. Physiol 16 423
3 SCHER A M A C YOUNG A L MALMGREN & R R PATON 1953 Spread of electrical activity through the wall of the ventricle Circulation Research 1 539
4 SCHER A M A L MALMGREN & R. V ERICKSON 1955 Activation of the interventricular septum Circulation Research 3 56



FIGURE 1 Position of the needle electrode in the ventricular wall during the experiment The bipolars in this position are shown in FIGURE 8

(1) *Sufficient length* The tip of the needle electrode must be in the ventricular cavity during all phases of cardiac activity

(2) *Smoothness of outer surface* The mechanism of the heartbeat results in systolic increase in thickness of the ventricular wall thus causing muscle layers in contact with the shaft of the needle to move along this shaft To avoid any interference with this movement the body of the needle is carefully polished and great care is taken that the small terminals do not protrude

(3) *Fixation' at the epicardial surface* The housing of the needle electrode in which connections are made between the small silver wires in the shaft and the connecting wires for the registering apparatus rests on the epicardial surface during all phases of cardiac activity Since the systolic increase in thickness of the ventricular wall gives rise to movements the greatest of these therefore occur in the subendocardial layers The distance by which these latter muscle layers move along the needle electrode is dependent on heart size heart frequency and degree of dilatation of the heart

(4) *Small weight (2 gm)* To avoid excessive pressure possibly resulting in injury the weight is kept minimal

(5) *Fixation* To improve fixation slight pressure is exerted on the needle electrode housing by the connecting wires but the direction of the force applied is parallel to the needle itself When the needle is pressed to one side of the puncture canal injury and retardation of propagation of the excitation wave result

(6) *No spiraling* The terminals lie at one side of the shaft

Numbering of Terminals

The terminal lying in the cavity is called terminal No 1 The highest numbered terminal lies upon or close to the epicardial surface The polarity of the bipolars is so chosen that positivity of the highest numbered terminal results in an upward deflection in the record

Avoiding Natural Irregularities of the Heart Rhythm

In some instances the heart rate is kept constant by driving electrodes upon the auricular appendage

Method of Introduction

The needle electrode is introduced perpendicular to the ventricular surface The endocardium is then felt as a resistance The electrode is pushed toward the cavity until the housing rests on the epicardial surface and the tip is within the ventricular cavity After introduction of the needles sometimes up to 5 in number the thorax is closed and to keep the temperature constant the animal is placed on a heating pad If it is necessary to keep a portion of the heart exposed that part of the heart surface not used is covered by pads of cotton soaked in warm saline

Instrumentation

The registering apparatus is a high fidelity oscillograph with separate viewing and registering tubes

For *stimulation experiments* the stimulating apparatus used was specially designed for these purposes with very accurate delay, counting and synchronizer mechanisms With this instrument it was possible to deliver a square wave test shock of any duration and strength at any chosen moment in the cardiac cycle after a preset number of heartbeats A current source was used

Number of Experiments

Satisfactory experiments with 200 dogs where needle electrodes were introduced in many places were obtained All previous experiments with plunge electrodes or low frequency registering apparatus were discarded

For experiments on the goat 20 animals were used

Injury Caused by Introduction of Needle Electrodes

It is evident that injury alters profoundly the mode of excitation of the injured layers Therefore a critical analysis of this point is important The influence of the movements of the heart and artefacts due to this factor will be discussed later

Immediately after introduction of the needle electrode injury occurs on all intramural myocardial terminals (FIGURE 2) The unipolar complexes in the consecutive layers have a monophasic form caused by injury On the epicardial surface the R wave becomes larger than before injury the S wave diminishes and the intrinsic deflections occur later in the cardiac cycle These facts can be explained by assuming a functional blockade of the depolarization

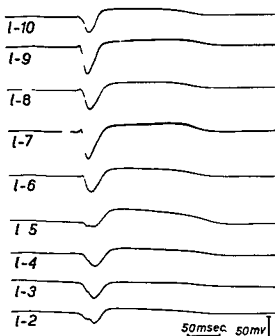


FIGURE 2 *Dog* Unipolar intramural complexes (*l* = leg) 2 minutes after the insertion of the needle No rapid deflections are present due to the injury effect The ST shift is the same at all intramural terminals

wave in the injured region[4] After 2 to 3 minutes the ST shift diminishes and fast components in the intramural complexes absent immediately after introduction gradually appear reaching their final value when the ST interval is isoelectric (FIGURE 3) We assume that the decrease in magnitude of the ST shift coincides with the return to normal of the fibers in the injured region

Strong arguments can be brought forward to give support to the assumption that our results are not influenced significantly by effects of injury

(1) Fast deflections (potential variation of 10 mv in 3 to 4 msec) previously absent during injury appeared in differential leads between 2 terminals lying at a distance of 0 1 mm or less

(2) After disappearance of the ST shift the strength interval curve for cathodal and anodal excitability of the intramural layers in contact with the terminals greatly altered during injury became the same as those of the surrounding epicardial muscle During injury the excitability for cathodal stimulation was diminished while excitability for anodal stimuli was enhanced

Movement artefacts due to variations in contact between electrodes and muscle give rise to characteristic irregularities of the base line With a good technique these irregularities are absent

The QRS complex is written before deformation of any significance has occurred during entrant phase and isometric contraction phase The ST segment and T wave for the most part are written during the ejection phase

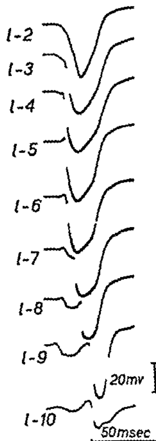


FIGURE 3 *Dog* Intramural unipolar complexes after the injury has disappeared (l = leg) The complex l 2 is just at the subendocardial layer adjacent to the cavity The rapid part of the intrinsic deflection occurs synchronously in the inner layers and successively in the outer layers A complex with an R wave of some height is present only in l 10

when the wall thickness is increased These latter portions are therefore written by layers that during QRS were lying closer to the epicardium

We did not succeed in mounting a sufficient number of differential electrodes into a needle with a diameter of not more than 1 mm

Microscopy Puncture Canal

After many hours of experimentation microscopic control of the puncture canal revealed the presence of a small zone of necrotic tissue about 0 1 mm in diameter immediately around the canal surrounded by a zone in which small bleedings and infiltration with leukocytes were present

Criteria for Acceptance of Tracing

The following criteria were applied for the acceptance of a tracing (1) absence of more than slight ST shift [6] (2) duration of the rapid part in the

intrinsic deflection not exceeding 3 msec (3) constancy in the form of successive complexes and (4) smoothly running zero line without artefacts

Time Relations

A study of the time relations of the excitatory process is possible only if the depolarization of the muscle layer in contact with the exploring terminal gives rise to a recognizable deflection signaling in the leads used the arrival of the excitation wave in that layer Therefore time relations can best be studied by electrodes with small distances betweeen the terminals for example 0 1 mm [6,7] With a differential electrode differentiation is performed in relation to space but not with respect to time [8] The height of the recorded potential is a function only of the properties of the activation front not of its velocity Only with spatial differentiation can the influence of activity in distant parts of the heart be excluded Therefore local activity determines form and polarity of the recorded complexes

The following facts are essential for the study of time relations

In intramural unipolar leads a rapid part in the large downstroke of the predominantly negative complex signals the arrival of the excitation wave in the muscle layers in contact with the exploring terminal

In bipolar leads two fast portions can be seen frequently on the upstroke and downstroke coinciding with the rapid portion mentioned above in the corresponding unipolar complexes and having the same significance The following evidence can be brought forward

In the intramural layers and at the epicardial surface a region is sought where

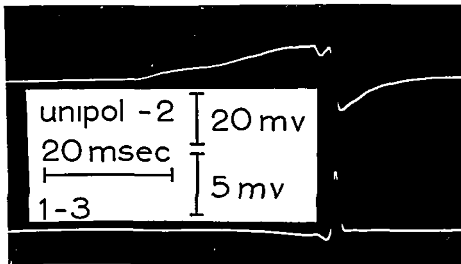


FIGURE 4 *Dog* A tripolar electrode is used The intrinsic deflection in the unipolar complex of the middle terminal falls exactly in the summit of the bipolar complex of the outer ones Note the symmetrical form of the latter

the excitation propagates with regular velocity A tripolar electrode consisting of 3 small terminals with equal surface area and of equal distances (½ mm) is brought in contact with these layers The bipolars between the successive terminals then have the same form and polarity and occur consecutively It can be seen in FIGURE 4 that the summit of the bipolar complex between the outer terminals coincides with the rapid portion of the unipolar complex of the middle terminal If the potential variations of the middle terminal are registered against a reference made by connecting the outer terminals a biphasic complex is found The large downstroke of that complex now coincides with the rapid part in the intrinsic deflection of the unipolar complex of the middle terminal

Activation Pattern of the Epicardial Surface

In an earlier part of the investigation it was thought that a careful analysis of the time relations of epicardial activation could give an insight into the intramural activation pattern With a small tipped electrode (0 1 mm) the epicardial surface was explored and the time of arrival of the excitation wave was carefully investigated The results of the work of previous authors[9] were confirmed The excitation has an over all direction from apex to basis In very small areas the propagation direction may differ and small excitation waves traveling in various directions are found The latest part activated is the posterobasal part of the left ventricular wall close to the posterior insertion of the ventricular septum

Intramural Analysis

An essential point is the location of the terminals of the needle electrode situated in the subendocardial region that is determination of the first terminal in the left ventricular wall

The unipolar cavity potential has a typical form (FIGURE 5) It is a rather symmetrical QS complex exhibiting no fast deflection with somewhat rounded summit

As outlined above the presence of an ST shift at a certain terminal does not necessarily indicate intramural position The first intramural lead point is found by the presence of a fast component in the QS complex It is possible however that the contact of a terminal with the trabeculae carneae causes the same phenomenon In this case this deflection disappears with slight rotation of the needle electrode Together with lifting the needle electrode this gives an indication of the position of the innermost lead points Not infrequently Purkinje spikes are found (FIGURES 6 and 7) which may indicate subendocardial position if the form of the consecutive bipolars supports this deduction

With the routine obtained in many experiments it proved possible to predict the position of the needle electrode in relation to the trabeculae carneae and the papillary muscle If the needle was situated in the papillary muscle the tip terminal did not register a cavity potential and the lead points at the tip of the needle electrode recorded complexes pointing to activation in the direction from endocardium toward the cavity (FIGURE 8)

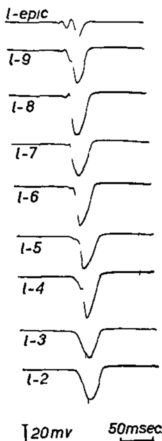


FIGURE 5. *Dog.* Epicardial and unipolar intramural complexes. *l*-2 and *l*-3 are cavity complexes. *l*-4 is the first terminal within the wall. A small R wave is shown for the first time in *l*-7, enlarging toward the epicardium.

Morphology of Unipolar Intramural Complexes of the Left Ventricular Wall

The form of the unipolar complexes depends on that portion of the ventricular wall where insertion has occurred (FIGURES 3 and 5). In all cases except when a papillary muscle is punctured the unipolar complexes are completely negative or nearly so. Sometimes a small initial positive deflection is found preceding the large negative one. In all complexes a fast component in the downstroke of the QS complex is visible (FIGURE 9). There may be some notching preceding or following this downstroke but in most cases it is slight. In the intramural layers lying closer to the epicardium small embryonic R waves frequently notched are visible also followed by a fast deflection. The rapid part of the intrinsic deflection can fall at any point in the downstroke of the unipolar complex (FIGURE 5)[8, 10]. Before the R wave in these layers a broad slow negative deflection sometimes showing notches is present.

Figure 6 *Dog* All bipolar complexes are compared with the Purkinje spike in lead 3-4 Terminal 3 is the first point in the wall 4-5 and 5 6 are small endocardial complexes 6 7 is a reversed complex 8 9 and 9 10 are well-developed muscle complexes

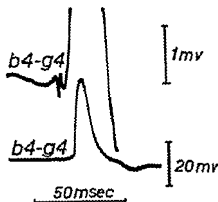


Figure 7 *Dog* Complex between 2 endocardial terminals of 2 needles The very small spike in the lower tracing was enlarged twentyfold in the upper tracing It shows a fast complex immediately preceding the muscular depolarization complex In the lower tracing the Purkinje spike can be seen as a small deflection preceding the muscular depolarization complex by 10 msec This is only an apparent delay because it is absent in the upper tracing

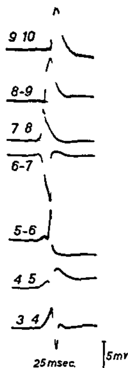


FIGURE 8 *Dog* Terminals 3 4 5 and 6 are situated in papillary muscle Bipolar leads 3-4 and 4 5 show papillary muscle complexes

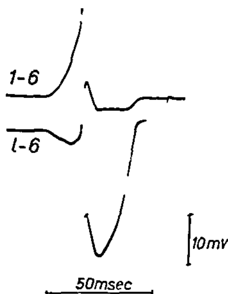


FIGURE 9 *Dog* Bipolar intramural lead between a terminal immediately adjacent to the endocardium and an intramural terminal (6) The unipolar lead of terminal 6 shows a sharp deflection (intrinsic deflection) occurring synchronously with the fast deflection in *l* 6 (*l* = leg)

Only in the subepicardial layers (3 to 4 mm under the epicardium) does the R wave gradually reach the height of the R at the corresponding epicardial surface

In many instances the intrinsic deflections of the inner layers occur at nearly the same time

In the outer layers the time differences are larger and the terminal closer to the epicardium is activated after the underlying terminal Formulated in another way the intrinsic deflections in the inner layers occur nearly synchronously while those in the outer layers occur consecutively[8, 10, 11]

The duration of the rapid part of the intrinsic deflection of the intramural terminals is very small from 2 to 5 msec The potential drop occurring during this very small time interval amounts to 20 mv

The best way to reconstruct the intramural excitation pathway would be to introduce many electrodes into the heart wall[14] It is apparent that the combined effects of too many needle electrodes of the type we use may alter the way of excitation and impair myocardial contractility As many as 6 may be used in our experiments

Intramural Bipolar Leads

These leads between 2 terminals ordinarily lying on a distance of 2 mm give accurate information on the time relations of the excitation process in the layers in which they are situated In this type of lead the local effects predominate and the extrinsic effects are reduced The form of the complexes registered gives additional information on the mode of activation and the direction of the excitatory process

The form of the bipolar complexes in the inner layers (FIGURES 6 and 10) is dependent on the depth of penetration of the Purkinje system This varies in different dogs and in different places of the same heart

In the Purkinje activated layers small complexes of about 5 to 10 mv are found In some instances they are notched In these layers mostly up to two fifths of the thickness of the ventricular wall the consecutive bipolar complexes occur synchronously

In FIGURE 6 bipolar complexes are shown with a Purkinje spike occurring at the endocardial terminal of the needle electrode taken as a reference The intrinsic deflections occur synchronously from terminal 4 to terminal 8 and consecutively thereafter

The morphology of the complexes in the outer layers can be explained by representing the excitation front in the outer layers as a dipole layer traveling with nearly constant velocity in an epicardial direction No retardation of propagation velocity of any significance toward the epicardial surface can be found The distance between the sources and the sinks of this boundary is about 1 to 1½ mm This value given as an approximation can be found with a needle electrode in which 8 small terminals are regularly spaced over a 3 mm length Registering the action potentials between two adjacent terminals and then gradually augmenting the distance one finds that the height and width of the registered complexes increase up to a distance of 1 to 1½

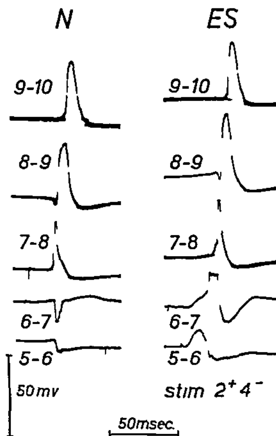


FIGURE 10 *Dog* Bipolar leads of normal beats and extrasystolic beats during endocardial stimulation Terminals 3 and 4 are used as stimulating electrodes Only the muscle fibers are activated From 7 on the complexes have the same form and time course during normal and extrasystolic beats The reversal of 6 7 pointing to activation from 7 to 6 disappears during endocardial stimulation and makes place for a complex pointing to muscle conduction from 6 to 7

mm between the electrodes This is the minimal distance between 2 terminals on which the maximum voltage caused by the excitation of the outer layers can be registered Beyond this value only the width of the complexes increases

The inaccurateness of this figure is caused by the usually small angle formed by the line of propagation direction and the line on which the terminals are lying

The value for the dipole length agrees very well with the duration of the rapid phase of the intrinsic deflection (3 to 5 msec)

Depth of Synchronous Activation

In the area where most of our experiments were performed—the area bounded by a line 1 cm apical of the sulcus atrioventricularis the left side of the ven

tricular septum and the lateral part of the left ventricular wall between the insertions in the papillary muscles—the depth most frequently found was two fifths of the diastolic thickness of the wall In some instances only 2 or 3 of 8 terminals showed successive activation (FIGURE 6)

The depth of the penetration in other parts of the ventricular wall varies At the apical side 10 experiments were performed Here the insertion in the papillary muscle and the presence of the ventricular septum and the trabeculae carneae make the interpretation of the results of our technique difficult (FIGURE 8) At the basal one third of the ventricular wall the same depth of penetration was found but in about 25 per cent of the places examined in that region there appeared to be complete absence of Purkinje penetration In the remaining areas the depth of penetration was somewhat less than in the middle part

Spatial Analysis of Activation Front

The construction of isochronic planes makes it possible to estimate the angle the excitation front makes with the endocardial and epicardial surface At the lateral part of the left ventricular wall this angle has a small magnitude approximately 5 to 10° For the purpose of direct measurement of this angle two or more needle electrodes were introduced in an apico-basal direction Terminals exhibiting the same spatial relations to the oncoming excitation wave will show potential fluctuations of the same magnitude or nearly so and therefore will show small differences Those terminals separated by ventricular tissue in which during activation there is set up a boundary that is traveling for some time in a direction more or less coinciding with the connecting line between the exploring terminals will show larger potential differences

The following explanation is given for the occurrence of this small angle in the left ventricular wall the endocardial layers are activated in an apico-basal direction Small excitation waves arrive from many points in the endocardial layers In the outer layers only muscle conduction is present those layers closer to the apex being activated earlier than those lying at the basal region The impulse traveling in the outer layers approaches the epicardium slowly because of the muscle conduction The time difference between two points lying in a line from apex to basis is determined mainly by the much higher velocity of impulse conduction through the Purkinje system This time will be small compared with the time required for the activation front to reach the epicardial surface The small angle therefore is caused by this difference in velocities in the two systems

Differences in the thickness of the ventricular wall and in the depth of penetration of the Purkinje fibers contribute to the exact magnitude of the angle

If the excitation front were a straight boundary of a simple form it could be expected that at the epicardial surface of the lateral part of the left ventricular wall excitation at every point would be in an apico basal direction The deviation of excitation direction found in many places at the epicardial surface can be explained by assuming that small bulges are present in the excitation front A bulge in the front arrives first at the epicardial surface If we measure from the epicardial surface we gain the impression that from this first reached part

a small excitation wave travels some distance in every direction until it collides with the excitation wave coming from other points. The small angle renders useless the determination of the propagation velocity of the excitation wave at the epicardial surface during normal beats. The values found are too high. For an exact determination of propagation velocity one must be sure that the line between the terminals used is parallel to the real direction of propagation of the excitation wave. When both lines intersect and make an angle, the measured propagation velocity is virtual and increases depending on the angle between both lines.

The Determination of Propagation Velocity

To determine the conduction velocity of the excitation wave and its relation to fiber direction, two successive terminals of a needle electrode were used as stimulating electrodes. The remaining terminals were used for successive bipolar leads. The needle electrode was introduced in the outer layers of the ventricle parallel to the epicardial surface. The angle made by the needle electrode and the fiber direction was measured. The heart rate was kept constant by driving electrodes sewn to the auricular appendage and the extra stimulus was given between the bipolar stimulating electrodes. In this way the delay of the extra stimulus could be measured accurately.

The form and polarity of the extrasystolic bipolar complexes from terminals surrounding the point of stimulation demonstrated that conduction of the extrasystolic beat occurred from the stimulation electrodes through the surrounding ventricular myocardium. At a distance of about 1 to 1½ cm from the stimulating electrodes the bipolar complexes had another form. It was assumed that these parts of the ventricular myocardium were activated by the Purkinje system, that is, by the excitation wave spreading inward from the subepicardial point of stimulation.

In about 100 determinations in 10 dogs conduction velocity was found to be independent of the direction of ventricular subepicardial muscle fibers.

Genesis of R Wave

At this point it is possible to give an analysis of the genesis of the R wave and an explanation of its presence in the outer layers only. The following factors must be taken into consideration.

(1) *The density and depth of penetration of the Purkinje fibers into the ventricular wall.* After traversing the large bundles the excitatory process arrives at the endocardial surface and the inner layers, where many islands of activation, one at every transition between specialized fiber and muscle, will be set up. These intramural islands are mostly closed surfaces and therefore are without external electric fields except in islands bounded by the endocardial surface. A positivity in a unipolar lead can occur only if a dipole boundary approaches the terminal considered.

Owing to cancellation of the electrical effects of the many fronts traveling in all directions, no R waves will be found in these layers. The trabeculated and intricate structure of the inner side of the ventricular wall is a contributing factor.

(2) *The absence of an R wave in regularly activated muscle layers at the anterior side* This phenomenon can be explained by the fact that the lead points in this area are situated at the negative side of the dipole layer traveling in a posterior basal direction in the ventricular septum and in the lateral and posterior side of the ventricular walls

(3) *The role of the ventricular septum* Investigators who made an extensive analysis of the mode of activation of the ventricular walls disagree in their results [13, 14] Our experiments [10, 19] so far as the ventricular septum is concerned, are limited to the registration of the potential differences between the left and right septal surfaces In nearly all places examined a positivity of the right side of the septum in relation to the left side was observed This points to an excess of activation from left to right thus augmenting the negativity in the left ventricular cavity In spite of the distance of the septum from the exploring electrode we believe that the possibility of an influence of septal activation cannot be ignored Also, the negativity of the cavity is a contributing factor

Extrasystoles[10, 15]

With the stimulating apparatus and methods described [20] and using two terminals of the needle electrodes as stimulating electrodes extrasystoles could be elicited from all desired places of the left ventricular wall and the way of excitation could be traced There was a difference in the response of the muscle layers in direct contact with and immediately surrounding the stimulating electrode (proximal part) and the response of the remaining part of the ventricles (distal part)

When the stimulating terminals were placed in the endocardial layers in the proximal part an excitation wave was set up propagating in all directions from the point of origin with constant velocity (FIGURE 10) These layers were therefore activated by muscle conduction In one instance the stimulating current directly stimulated the Purkinje fibers in the proximal region (FIGURE 13) This experiment is discussed later In most cases the remaining part of the heart (distal part) was activated by the Purkinje system picking up the excitation wave at a distance of ½ to 1 cm from the stimulating terminals

Stimulation of the epicardial layers gives rise to excitation in reverse direction in the proximal area (FIGURE 11) The excitation wave travels with constant velocity from the epicardium toward the endocardium The muscle layers in contact with the needle electrode previously activated by the Purkinje system are now activated by muscle conduction only The Purkinje system is responsible for the distribution of the excitation wave to the remaining part of the heart

These experiments support the hypothesis that the inner layers of the left ventricular wall have the peculiar activation pattern not only because of the intricate anatomical structure at the endocardial surface but also because of the presence of a rapid distributing system penetrating a certain distance into the wall In conclusion we may state that our results support the assumption that the endocardial surface is activated within a very short time interval by

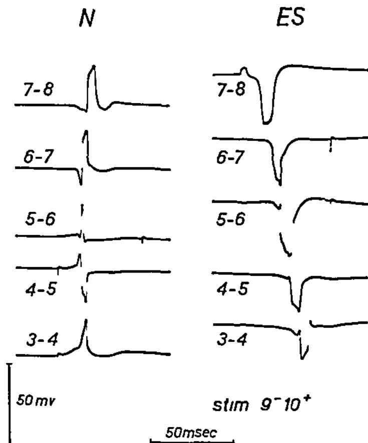


FIGURE 11 Dog A good example of epicardial stimulation where a regular front is propagating from epicardium to endocardium The complexes have a greater width than with normal beats This is caused by the fact that the front is now passing exactly in the direction of the needle This is not the case with normal beats With normal beats a small angle is present between the direction of the needle electrode and the direction of propagation Terminals 9 and 10 are the stimulating electrodes

the Purkinje system distributing the excitation wave to many places at the endocardial surface and in the subendocardial layers The basal parts of the left ventricular wall are activated in many places somewhat later than in the remaining parts usually 5 msec

The anatomical picture given by Jane S Robb *et al* [16] accounts completely for our results These investigators demonstrated that in the heart of the dog Purkinje fibers penetrate into the left ventricular wall and activate certain areas

Reversal Phenomenon (Figure 12)

In some cases a peculiar phenomenon is found In a muscle layer commonly lying between synchronously and successively activated layers the polarity of

the bipolar complex points to conduction from the epicardium toward the endocardium that is toward the ventricular cavity a phenomenon commonly found in the papillary muscle In about 75 per cent of the regions examined this conduction was most frequently present in the middle part of the left ventricular wall The genesis of this complex is still doubtful but the following observations are pertinent to the problem

(1) During extrasystoles elicited between terminals lying closer to the epicardium of the same needle electrode the polarity of the complex does not change

(2) During endocardial stimulation the polarity of the phenomenon commonly reverses pointing to activation in endocardial epicardial direction

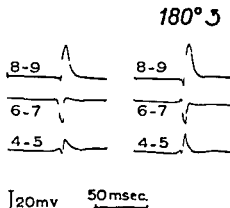


FIGURE 12 *Dog* Bipolar complexes when the needle electrode is turned 180° No significant differences in the form and time occurrence of the complexes are seen Also the reversed complex is unchanged

except when the Purkinje system is activated directly by the stimulating current depending upon current strength (FIGURE 13)

(3) Turning the needle 180 does not change the time relations between the muscle layer activated in a reversed direction and adjacent layers (FIGURE 12)

(4) In animals in which the anatomical structure is well known (the goat for example) several reversals may be present at the same needle electrode

Stimulation of Purkinje Fibers

Many experiments on dogs were performed to stimulate the subendocardial Purkinje fibers directly If the inner layers are activated by Purkinje conduction direct stimulation of these fibers by the stimulating current should give rise to complexes with the same time relations as during normal beats

Many experiments were unsuccessful because the Purkinje fibers causing a typical spike at a certain terminal disappeared after the first extrasystolic beat It may be presumed that the mechanism of the contraction of an extrasystolic beat is different from that of a normal beat especially in the region where stimulation occurs

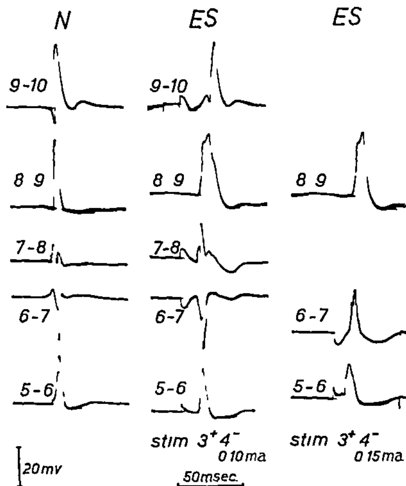


FIGURE 13 *Dog* Important experiment to show the influence of the Purkinje system Complex 6 7 is a well developed reversal complex between 2 normal bipolar complexes (5 6 7 8) with a polarity pointing to activation in endocardial-epicardial direction During an endocardial stimulus of 0 1 mAmp the Purkinje system evidently is activated and the reversal phenomenon still exists With 0 15 mAmp the muscle also is directly activated and the reversal phenomenon disappears Note also that both in normal and Purkinje extrasystolic complexes 5 6 and 6 7 have their summits nearly at the same time whereas in the third row when myocardial conduction is present complex 6-7 follows 5 6 after 11 msec

In one experiment the spatial relationship of a Purkinje fiber to the stimulating terminals remained constant (FIGURES 13 and 14) During stimulation bipolar complexes could be found with the same time relations and form as the normal beats A reversed activated layer did not change its activation pattern during the extrasystolic beat In the outer layers the bipolar complexes were somewhat broader because here the direction of propagation of the extrasystolic wave was parallel with the needle electrode and not so in the normal beat where both lines enclosed a small angle Microscopic control of the

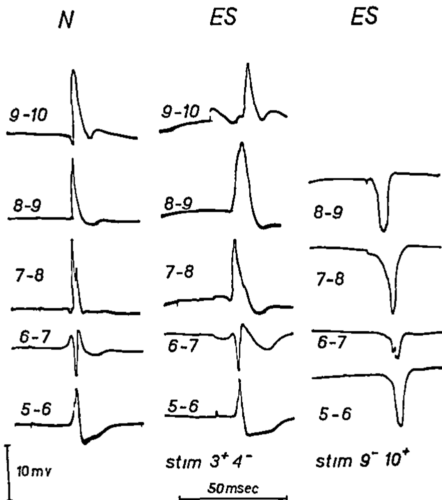


FIGURE 14 *Dog* As in FIGURE 13 except that an epicardial extrasystole has also been made All bipolar complexes have a reversed polarity Only the complex 6 7 which was originally reversed has kept its polarity With epicardial stimulation all bipolar complexes follow each other continuously

region where terminal 4 was lying revealed that a strand of Purkinje fibers was lying immediately around the puncture canal in that region

If the Purkinje system penetrates into the left ventricular wall it might be supposed that with increasing distance from the endocardium the meshes of this system become wider toward the epicardial surface An activation wave originating from a Purkinje fiber can travel in all directions that is also in an epicardial endocardial direction from the point of transition into a ventricular muscle fiber until it collides with tissue activated by activation waves originating from adjacent Purkinje fibers If the meshes are wide enough a reversed complex can be found between two of our terminals

Excitation in Goats

Our estimation of the intramural extension of the Purkinje fibers in the dog based on physiological experiments lacks anatomical control It has therefore been necessary to repeat these experiments on an animal with better known anatomical structure of the Purkinje system so that the principles on which anatomical deductions are made can be tested

Ter Borg[17] and Meyling[1] have investigated the hearts of many ruminants Their results with respect to the heart of the goat are pertinent to our problem because that animal has been used for our own subsequent experiments Ter Borg and Meyling injected the goat Purkinje system with India ink and later clarified the heart muscle by using the Spalteholz method Their results can be summarized in the following way

The Purkinje fibers form a network throughout the whole myocardium A division into left and right Purkinje systems is nowhere to be found There

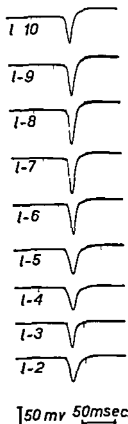


FIGURE 15 *Goat* Unipolar intramural complexes (*l* = leg) The needle electrode is introduced at a place on the lateral part of the left ventricular wall where a QS complex is present at the epicardial surface Note the symmetrical form No fast parts in the down stroke of the QS complexes are found

is a continuity of the Purkinje network both throughout the septum and along the parietal walls The density of the Purkinje system diminishes in the basal region of the ventricular walls and the septum In the septum the fibers at the basal part do not originate from the main bundle lying there but from points situated in a more apical direction

So far as the left ventricular wall is concerned our experiments with goats are readily explained by this anatomical picture

The epicardial complexes have a peculiar form In the lateral part of the left ventricular wall the area most suitable for the introduction of the needle electrode Q S complexes are found The intrinsic deflections are less well developed than in the dog and are not recognized as easily (FIGURE 15) The bipolar complexes of the successive layers begin at nearly the same time and also end almost synchronously The polarity in the successive layers differs and in some places it reverses pointing to an excess of activation in epi cardial endocardial direction (FIGURE 16) In the outer layers well-developed complexes are sometimes present pointing to activation toward the epicardial surface

These findings can be explained by the spatial distribution of the Purkinje system

The Purkinje system penetrates into the left ventricular wall nearly to the

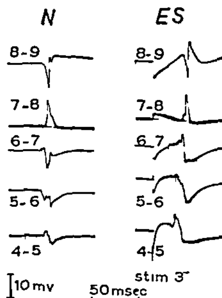


FIGURE 16 *Goat* Complexes in the left row occur during normal beats In the right row complexes occur during endocardial stimulation (3⁻) Bipolar complexes 7 8 and 8 9 which show complexes of opposite pola ity during normal beats retain the same form and polarity during the extrasystolic beat The time relations too do not alter during the ex trasy tole This supports our hypothesis that at a certain distance from the stimulating elec trode the Purkinje system is activated by the muscular depolarization front traveling between 4 5 5 6 and partly between 6-7

epicardial surface It is responsible for a rapid distribution of small excitation waves at many levels of the ventricular wall The portions of heart muscle filling up the meshes are activated from these points At many places Purkinje spikes in different layers can be found pointing to great velocity of distribution These Purkinje spikes are sometimes followed by well developed muscular complexes after a 10 msec delay This is only an apparent delay however because with large amplification it is absent The Purkinje spike is followed immediately by a muscular depolarization complex This build up time also present in the dog (FIGURE 7) is caused by the gradual increase in voltage resulting from the increasing number of fibers activated after transition of the excitation wave from the Purkinje fiber into myocardial fiber

Extrasystoles in Goats

The experimental procedure used for goats was the same as that used for dogs

Endocardial stimulation (FIGURES 17 and 18) In the endocardial layers stimulation may give rise to depolarization complexes occurring almost synchronously when the Purkinje system is stimulated directly by the stimulating current In layers where the stimulating electrodes are situated complexes

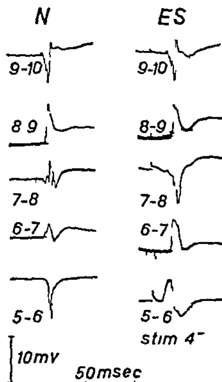


FIGURE 17 Goat Endocardial stimulation (4) The muscular bipolar complexes in the neighborhood of the stimulating terminals (5 6 and 7) are well developed and occur successively Terminals 8 9 and 10 are situated in Purkinje activated layers

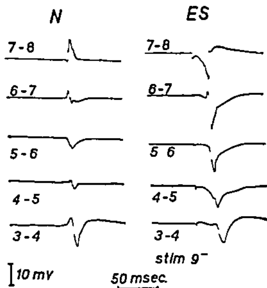


FIGURE 18 *Goat* Bipolar leads Normal complexes and epicardial extrasystoles The normal complexes have an irregular form and have no simple time relation The extrasystoles show mainly muscle conduction the complexes following each other in time from epicardium to endocardium In different layers small activation waves propagating in an epicardial endocardial direction are still present when the underlying muscle layer is already activated The propagation velocity is approximately 20 cm per second The Purkinje system is activated in an epicardial endocardial direction

found in bipolar leads in most instances show the form and time relations of a beat predominantly propagated by muscular conduction The bipolars are broad showing more notches than those in the dog and occurring consecutively At some distance for instance 4 to 6 mm from the stimulating terminals complexes that have a form pointing to Purkinje activation are found They have a smaller multiphasic voltage that occurs synchronously in the successive leads A reversal occurring at a certain layer can also be present during the extrasystolic beat—the Purkinje fibers have activated this layer in a nearly normal way ahead of the excitation wave traveling in the inner layers (FIGURE 17)

Epicardial stimulation The over all direction of the excitation wave in epicardial stimulation is from outside to inside but the time of occurrence of the bipolar complexes is different from that in the dog In the latter case a sharply defined boundary is present during excitation but here the time relations make it possible for the Purkinje system to distribute the impulse in an antidromic way There is partial muscle conduction and partial Purkinje conduction

Conclusion

Our experiments clearly point to the conclusion that the inner layers of the left ventricular wall are activated by Purkinje fibers penetrating over a variable distance The exact mode of excitation is not known The size of the area

activated by one fiber cannot be ascertained However this pattern is one of the factors responsible for the presence of predominating negative QS complexes in the inner layers and the great influence of the subepicardial layers on height and width of the R wave

In the dog the influence of epicardial and endocardial extrasystoles on the form of bipolar leads could be explained by assuming that in the area stimulated the Purkinje system as a rule was not activated and muscle conduction was present altering the form and polarity of the bipolars in the inner layers

The boundary set up during an extrasystole traveled continuously from point of stimulation to the epicardial or endocardial surface No retardation was found in the bipolar complexes in the outer layers during these extrasystoles *The region at a distance of more than ½ to 1 cm from the stimulating* electrode was activated by Purkinje fibers in the same manner as during the normal beat

After having developed the technique described it proved possible to study many problems in normal and pathological conditions An exact determination of the course of excitability during the cardiac cycle showed important facts There is a constant time difference between depolarization and repolarization in the intramural layers when the repolarization is measured at the length of the absolute and relative refractory periods The effect of mechanical injury on excitability or of injury caused by ligation of the coronary artery hypothermia and frequency changes could be studied The mode of excitation in infarctions is being investigated in this way

During the publications of our experiments other investigators have used comparable methods sometimes with nearly the same results[6] sometimes disagreeing with our findings in some respects[12] Also criticism on some points has been offered[18] In this work however the electrodes used are unsuitable for the examination of the reversal phenomenon Therefore in the facts presented above, more stress than usual has been laid on the methodology and on the limitations of this method

We have always been conscious of the difficulties of the study of the intact heart Consequently we have checked and rechecked the results of almost every *experiment over the years We feel certain that every precaution has* been taken to avoid mistakes and we feel qualified to state that some of the other published tracings cannot meet the criteria we have used for the selection of our own We hope that we have demonstrated the applicability of our technique and we believe that it will be of great value in the analysis of the excitation pattern in normal and pathological conditions

Acknowledgments

We express our sincere thanks to R Th van Dam for his great help in the preparation of this manuscript and for his permission to use some of the data of experiments in which he participated We also express our appreciation to A van Lier S Berreklouw H Koster M van der Kooi A I Hakman and J van Gool for their assistance during the experiments H T Deelman s cooperation in performing the microscopic examinations is greatly appreciated

References

1 Lewis T & M A Rothschild 1915 Phil. Trans. Roy Soc B206 181
2 Wilson F N F F Rosenbaum & F D Johnston 1947 Interpretation of the ventricular complex of the electrocardiogram Advances in Internal Med 2 1-64
3 Durrer D 1952 Experimenteel onderzoek naar het verloop van het activatieproces in de hartspier Thesis Scheltema & Holkema. Amsterdam Holland
4 Sodi Pallares D 1951 Nuevas Bases de la Electrocardiografia. 3rd ed La Prensa Medica Mexicana.
5 Sodi Pallares D A Bisteni G A Medrano & F Cisneros 1955 The activation of the free left ventricular wall of the dog s heart Am Heart J 49 587
6 Clement C 1912 Z Biol 58 110
7 Durrer D & L. H van der Tweel. 1954 Spread of activation in the left ventricular wall of the dog II Am Heart J 47 192
8 Durrer D & L. H van der Tweel. 1953 Spread of activation in the left ventricular wall of the dog I Am Heart J 46 683
9 Harris A. S 1941 Am J Physiol 134 319
10 Durrer D L H van der Tweel & J R Blickman 1954 Spread of activation in the left ventricular wall of the dog III Am Heart J 48 13
11 Kennamer R J L Bernstein M H Maxwell M Prinzmetal & C McK Shaw 1953 Studies on the mechanism of ventricular activity V Intramural depolarization potentials in the normal heart with a consideration of currents of injury in coronary artery disease Am Heart J 46 3 9
12 Scher A M A C Young A L Malmgren & R R. Paton 1953 Spread of electrical activity through the wall of the ventricle Circulation Research 1 539
13 Scher A M A C Young A. L Malmgren & R V Erickson 1955 Activation of the interventricular septum Circulation Research 3 56
14 Sodi Pallares D M I Rodriguez L O Chait & R Zuckermann 1951 The activation of the interventricular septum Am Heart J 41 569
15 Scher A M & A C Young 1955 Spread of excitation during premature ventricular systoles Circulation Research 3 535
16 Robb J S C F Kaylor & W G Turman 1948 Am J Med 5 324
17 Ter Borg H 1941 Acta Neerl Morphol 4 97
18 Massumi R A A. Goldman L Rakita K Kuramoto & M Prinzmetal 1955 Studies on the mechanism of ventricular activity Am J Med 19 832
19 Durrer D L H van der Tweel S Berreklouw & L P van der Wey 1955 Spread of activation in the left ventricular wall of the dog IV Am Heart J 50 860
20 van Dam R Th D Durrer J Strackee & L H van der Tweel 1956 Excitability cycle of the dog s left ventricle Circulation Research 4 196
21 H A Meyling To be published

THE ACTIVATION OF THE INTERVENTRICULAR SEPTUM IN THE DOG'S HEART UNDER NORMAL CONDITIONS AND IN BUNDLE BRANCH BLOCK

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A recent article on the activation of the interventricular septum[1] disclosed several features that seemed at variance with the results reported in our previous papers. This afforded us an excellent opportunity to present our latest data and views derived from experiments using improved techniques. Heretofore the criticism leveled at our methods fell into the following categories: (1) the exclusive use of unipolar leads, (2) the distance separating the electrodes in close bipolar leads, and (3) the use of direct writing machines. While we formerly concurred with these objections on theoretical grounds, recently we have subjected these points to experimentation and to mathematical analysis and have come to the conclusion that they are not significantly valid. Further discussion of these matters will be presented later. Nevertheless, to avoid all possible objections, we redesigned our experimental approach to allow for all of the criticisms listed above. From this vantage point we can engage in a discussion of the more pertinent problem, the basic conceptual disagreement that now seems to exist as to the manner of septal activation. These differences extend also to free wall activation, but since Durrer, in a recent excellent paper, substantially confirmed our results in this field, we do not propose to discuss free wall activation at this time.

Material and Methods

(1) The experiments described were limited to 20 dogs. The number was kept deliberately small because the work confirmed our results previously obtained in over 100 dogs.

(2) The anesthesia, the preparation of animals, and the introduction of electrodes were as previously described in other experiments.[3, 4]

(3) A Dual Beam Dumont Type 322 oscillograph was used in conjunction with Grass Pre amplifiers model P-4 A. Recordings were made with a Grass model C-4 C high speed camera, which allowed us to work at speeds up to 1000 mm./sec. We rarely employed the latter speed, finding speeds of 250 and 500 mm./sec. more satisfactory for our purposes.

(4) *Description of electrodes.* Recently one of us (Gustavo A. Medrano) devised an extremely acceptable electrode. A B D trochar No. 15 16 was used for the shaft, and 10 to 12 holes of a diameter 0.5 mm. were drilled along the length of the trochar at a separating distance of 1 mm. (FIGURE 1). Into each drilled aperture 2 extremely fine insulated copper wires were threaded through the length of the shaft. The entire assembly was then coated with liquid Lucite, and a layer of lacquer was applied. The completed unit was tested with an ohmeter for any short circuits between any 2 wires or any wire

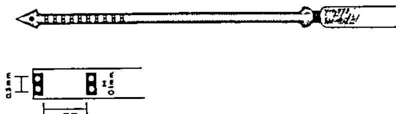


FIGURE 1

and the trochar The finished assembly then represented 10 to 12 sets of extremely close bipolar leads with an interelectrodal distance of 0 3 mm including the diameter of the wire

The use of copper wire in this type of work could be objected to because this metal easily becomes polarized in electrolytic solutions A Rosenblueth (personal communication) of the National Institute of Cardiology Mexico City has proved experimentally that this polarization effect varies in proportion to the type of condenser used in the amplifiers Since very high resistances are used the effect is negligible In our work this effect would be of significance only in the very low frequency components (T RS-T) of the tracing Rapid deflections however such as the intrinsic phenomena of the bipolar leads the apex of which marks the arrival of the activation process remain essentially unmodified the polarization effect being negligible According to Rosenblueth the distortion produced in unipolar leads under these conditions makes them less reliable Despite this in our experience with unipolar leads we have not noted any overshoot For that reason we feel the morphologies obtained in unipolar leads are generally valid

To prove that the polarization factor is negligible when we were working with our type of amplifiers and cathode ray oscillograph we recorded a unipolar lead in the anterior wall of the left ventricle using the following different materials for electrodes (1) unpolarizable silver (2) polarizable copper (3) polarizable steel (4) lightly polarizable or unpolarizable chlorated copper

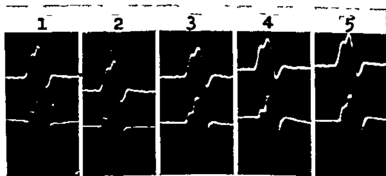


FIGURE 2 Tracings recorded with electrodes of the following materials 1 silver 2 copper 3 steel 4 chlorated copper and 5 cotton attached to silver wire

and (5) nonpolarizable cotton attached to silver wires As can be seen in FIGURE 2 there are no changes in the unipolar morphologies and the figures are identical in all instances

(5) Each experiment was performed with both bipolar and unipolar leads We took this additional precaution because some authors[4, 5] have stressed the difficulties encountered in determining the arrival of the activation wave when using exclusively unipolar leads In fact this was our concept until recently but we are now aware of the intimate and mathematical relationship that exists between unipolar and bipolar leads (see *Discussion*)

(6) Following each experiment the dog was sacrificed with the electrodes *in situ* Precise localization of each recording point was thereby established

Results

The following figures are representative tracings of the results obtained in the several experiments mentioned

The right half of FIGURE 3 shows a schematization of the interventricular septum cut along its longitudinal axis Lines were drawn within the septal mass in an attempt to represent the electrical division of the septum (see *Discussion*) into those portions activated by the left and right bundle branches[3] Using the plunge electrode previously described bipolar tracings were recorded at the points illustrated The distance between point 1 and the left septal surface was 2 5 mm and the succeeding points were separated by a distance of 3 mm The width of the septum in this case was 21 mm At the left of the diagram lead II is recorded simultaneously with each of 5 contiguous bipolar leads obtained within the septal mass of the dog s heart In this experiment at the septal level explored the points were activated almost simultaneously

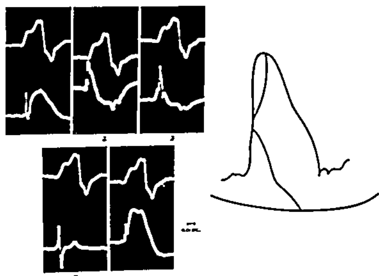


FIGURE 3 Lead II recorded simultaneously with each of the 5 contiguous bipolar leads obtained within the septal mass in a normal dog s heart

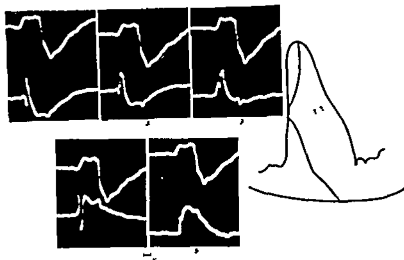


FIGURE 4 Lead II recorded simultaneously with each 1 of 5 contiguous bipolar leads obtained within the septal mass of a dog s heart with RBBB

and very early in relation to the onset of QRS in lead II In all the points explored activation was accomplished within 5 msec

Using the same preparation described above with the electrode position unchanged right bundle branch block (RBBB) was produced (FIGURE 4) Again complete activation occurred within 5 msec and the sequence of activation remained unaltered as compared to the control

From the same points unipolar tracings were recorded during RBBB Morphologically the complexes were entirely of the QS or RS type (FIGURE 5) These complexes are typical of the left septal mass after RBBB and they agree with our previously published findings[8] As shown later right septal morphologies during RBBB which are of the RS type with the R wave being broad and notched were not recorded in this experiment

In the next series of experiments to be described a different type of recording electrode was used (FIGURES 6 and 7) The electrode consisted of 2 very fine insulated wires closely bound to one another along their full lengths The lead ends of the assembly were used as close bipolar leads (interelectrodal distance of 0 5 mm) The electrode was introduced into the septum by crossing the free left ventricular wall and left cavity By carefully advancing the electrode across the septum it was possible to record at intervals of 1 5 mm In FIGURE 6 points 1 to 10 were explored with unipolar leads after producing RBBB The morphology of points 1 to 9 it will be noted is of the QS variety At point 10 a distance of 1 5 mm from point 9 the complex abruptly assumes the QRS form More than that the intrinsic phenomena of point 10 are inscribed during the ascending limb of the S wave of lead II whereas the intrinsic phenomena of all other points occur early during the upstroke of the R wave of lead II The same points were explored with bipolar leads (FIGURE 7) Points 1 to 9 were activated within 6 msec Point 10 on the other hand

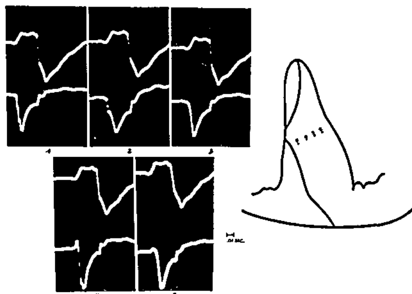


FIGURE 5 Lead II recorded simultaneously with each 1 of 5 unipolar leads obtained within the septal mass of a dog s heart with RBBB

was activated about 0 03 sec later Thus we see a marked delay between points 9 and 10 In point 6 we choose the uppermost part of the rapidly ascending limb as the point of arrival of the activation process not the center of the slurred apex

Points 8 and 9 in the bipolar experiment (FIGURE 7) can be criticized as the intrinsic phenomena are not well delineated at these locations This often

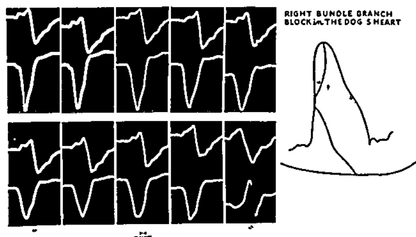


FIGURE 6 Lead II obtained simultaneously with each 1 of 10 unipolar leads recorded within the mass of the interventricular septum

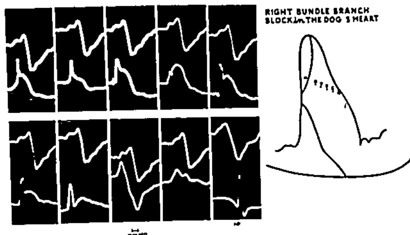


FIGURE 7 Lead II obtained simultaneously with each 1 of 10 bipolar leads recorded within the mass of the interventricular septum

happens in those points proximal to the boundary between right and left septal masses Since there is a good correlation between the intrinsic phenomena of unipolar and bipolar leads however (see *Discussion*) the unipolar records help us to identify the arrival of the activation process

In FIGURE 8 the schematic portion represents several aspects of the interventricular septum The central diagram is again the frontal aspect of the septum The 2 triangular figures are respectively the right and left septal surfaces seen sagittally The tricuspid and mitral valves are represented by the scalloped curves so placed as to indicate their location with respect to the septal surfaces

Point A in the illustration is seen to be anterosuperior An electrode containing 10 pairs of close bipolar leads each pair separated by a distance of 1 3 mm was passed horizontally across the septum at A As pictorially repre

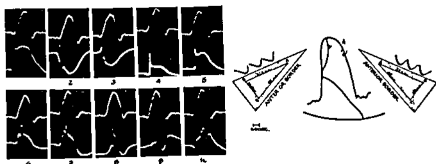
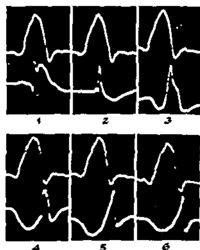


FIGURE 8 Lead II recorded simultaneously with each 1 of the 10 contiguous bipolar leads obtained within the septal mass in a normal dog's heart



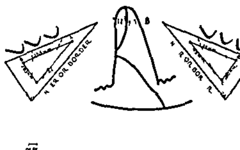


FIGURE 9 Lead II recorded simultaneously with each 1 of 6 contiguous bipolar lea obtained within the septal mass in a normal dog's heart

sented point 1 was in the cavity Subendocardial point 2 as can be seen fro the accompanying records was the first point to be activated Furthermor *activation spread at a varying speed (664 to 518 mm /sec) in a sequential le to right direction* The distance between points 2 and 10 was 11 6 mm an the corresponding interval between their times of activation was 0 022 se In FIGURE 9 electrode *B* was inserted at about the same level as electrode *A* but more posteriorly It will be noted from the diagrams that the 2 electrode are not exactly parallel The 6 close bipolar pairs of exploring electrode located along *B* were separated by the following distances points 1 2 1 mm points 2 3 3 mm points 3-4 1 7 mm points 4 5 1 7 mm , and point 5 6 1 7 mm The earliest site to be activated was point 1 and the lates was 5 the differential in time was 0 022 sec The computed speeds between th electrodes fell within a less narrow range (355 to 714 mm /sec) and the greate speeds were recorded near the left septal surface with progressive diminutio *as the right side was approached Points 4 5 and 6 which belong to the righ* septal mass were activated very late and were synchronous with some portio of the S wave in lead II In all our experimental work these regions hav been found to be the most delayed

FIGURE 10 is identical to FIGURE 9 except for the use of a camera speed o 250 mm /sec

FIGURE 11 shows the tracings derived from an electrode that was passe across the septum at point *C* The diagrams show it to be anterior but low Of the 8 recording pairs the earliest sites of activation were in the first 2 points The last point activated was point 8 The time interval between the earlies and latest points was 0 023 sec The speed of activation between the first 2 points was 1100 mm sec and 266 mm / ec between points 7 and 8 Thu *the speed was initially rapid and progressively decreased as the wave of activa*tion spread from left to right (see *Discussion*)

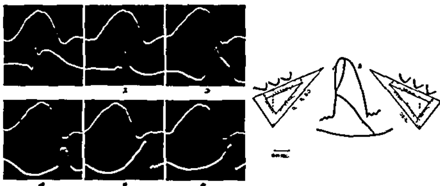


FIGURE 10 Lead II recorded simultaneously with each 1 of 6 contiguous bipolar leads obtained within the septal mass in a normal dog's heart

In each of the 3 previously discussed figures the distances between the explored points on the right and left septal surface are given in the diagrams Comparing the times of activation of the various points located along *A* *B* and *C* the left subendocardial points along *A* and *C* showed the earliest activation The intrinsic phenomena of these points were inscribed 7 and 9 msec respectively after the beginning of Q in lead II The left subendocardial electrode pair in location *B* while it preceded all of the adjoining pairs along *B* was activated 23 msec after the onset of Q in lead II The time differences between the earliest points of activation of *A* and *C* and the earliest points of *B* were 16 and 14 msec respectively In essence the left septal surface in its low anterior aspect falls into activation in less than 5 msec while the left posterosuperior portion is markedly delayed (in this experiment 23 msec after

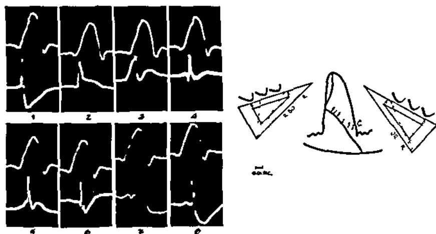


FIGURE 11 Lead II recorded simultaneously with each 1 of 8 contiguous bipolar leads obtained within the septum in a normal dog s heart

activity was noted in lead II) Despite the delay in the left posterosuperior portions it becomes even more profound as the right posterosuperior surface is approached The measured delay at point 5 along B was 45 msec The general spread of electrical activation in the normal septum could then be represented as a vector directed from left to right from below upward, and from front to back

FIGURE 12 shows the unipolar morphologies recorded in the high and posterior portions of the septum It will be noted that QR complexes are seen on both the right and left septal surfaces As the interior of the septum is explored RS complexes are recorded (points 3 and 4 of FIGURE 12)

Discussion

As stated in the introduction the primary purpose of this paper is to clarify certain areas of disagreement that now exist as to the nature of septal activation We propose to deal simultaneously with the problems encountered in this type of work and the conclusions reached on the basis of our experimentation The discussion can be facilitated by arranging the material in the following categories (1) relation between direct unipolar and close bipolar leads (2) septal activation (3) electrical partition of the septum (4) anatomical partition of the septum and (5) QR and QRS complexes in the high portions of the septum

Relation between direct unipolar and close bipolar leads In 1950[6] in the course of our investigations on the relationship between the types of leads mentioned above we arrived experimentally at an empirical correlation Stated simply the apex of the intrinsic phenomena of the bipolar record was generally within the last one third to one half of the rapid downward component of the

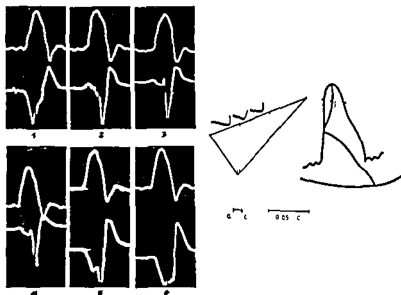


FIGURE 12 Lead II recorded simultaneously with each 1 of the 6 unipolar leads obtained within the septal mass in a normal dog's heart

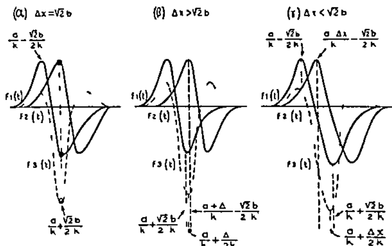


FIGURE 13 Relationship between close bipolar ECG $f(t)$ with its component unipolar leads $f_1(t)$ and $f_2(t)$ The nadir (lead connections reversed) of the bipolar lead under the conditions $\Delta x = \sqrt{2b}$ is synchronous with the apex and the nadir of the unipolar derivations (Δx = interelectrodal distance b = distance of electrode from activated muscle mass) Figure from Itatsu[8]

direct unipolar record The relationship can be amplified further as follows If bipolar contiguous leads are recorded simultaneously at the same location on the tissue it will be seen that in many cases the ascending limb of the bipolar leads is synchronous with the intrinsic deflection of the unipolar lead at the point activated first On the other hand the descending limb of the bipolar lead is synchronous with the intrinsic deflection of the unipolar lead at the point activated later [7]

Itatsu[8] has recently worked out mathematical formulas covering the relationship described above Its validity holds in most cases as can be seen in FIGURE 13 α The other examples β and γ describe other relationships for these leads and are not relevant to our present discussion It is only when unipolar complexes beginning with a Q wave (QRS QR) are analyzed that certain discrepancies become manifest FIGURE 12 illustrates this point—the black line superimposed on the unipolar records corresponds to the time of inscription of the intrinsic phenomena determined from close bipolar leads at coincident points It can be seen that in this type of morphology there is no close correlation between the intrinsic phenomena of close bipolar and direct unipolar leads

In the main both studies confirmed the unique value of the apex of the rapid deflection of the close bipolar lead in establishing the time of arrival of the activation process While in most cases unipolar records are closely related to the bipolar they find their real significance in the morphologic analysis of the spread of activation In our laboratory no study is complete without both types of derivation

The activation of the septum Scher *et al*[1] have studied septal activation by means of a multichannel oscillograph Numerous points with [illegible] um

were explored and synchronously recorded Isochronous planes were then drawn through those points that showed simultaneous activation A composite of such planes shows that septal activation commenced initially on the left septal surface which was followed subsequently by a smooth double envelopment of the septum by two activation waves proceeding from the left and right septal surfaces Eventually these two waves meet and cancel in the mid line of the septum In our studies we have been impressed with the great complexity of septal activation The relatively simple method used by Scher *et al* prompted us to repeat their experiments In so doing we were unable to reproduce the pattern of isochronous planes that they reported In addition as we shall see in the following section, the advancing activation fronts proceeding from the left and right septal surfaces do not meet in the mid line

We studied the conduction rate and our results in this area may be summarized as follows

(1) In some experiments in our series (FIGURE 3) the left septal mass in its middle one third was activated almost simultaneously

(2) In the subendocardial muscle near the middle one third of the left septal surface activation occurs almost simultaneously (infinite values for the conduction rate) This suggests that these points are not activated by any defined wave front but are separately and simultaneously activated through the Purkinje network Consider a subendocardial point and then on the same level a series of points within the septal mass each point being progressively farther removed from the subendocardium The computed rates of conduction at each of these points reveal an interesting relationship Beginning as practically infinite speeds at the subendocardium the speeds become finite and progressively slower[9] The explanation for this phenomenon is probably that the wave does not slow down as it traverses the septum but rather that speeds at any point are due to a composite effect of muscular and Purkinje activation What appears to be a slowing down is in reality a consequence of increasing scarcity of Purkinje fibers as the septum is penetrated more deeply This discussion gives some idea of the complexity of the problem and the guarded significance that must be assigned to any computed values of conduction rate

(3) In the upper one third of the septum we have found relatively slow and uniform conduction rates with morphologies similar to those described by Scher *et al*[1]

(4) The first regions to become activated are in the middle one third of the left septal surface This has been confirmed by several authors[1, 3] In our studies the latest regions to become activated are the high posterior portions of the right septal surface In FIGURES 9 and 10 it can be seen that the apex of the bipolar lead is inscribed simultaneously with the terminal portion of the S wave of the QRS complex of lead II The high posterior portion of the left septal surface is also delayed again suggesting sparseness of the Purkinje fibers in that neighborhood It is fair to state that the lack of information on the lower septal mass which is predominantly formed by the right septum is due to the fact that this area has not been well explored

(5) On the right septal surface the first region to become activated is at the

base of the anterior papillary muscle It follows then that, if the last region is high and posterior and the first is low on the septum, we may speak of the activation process of the right septal surface and the right septal mass (see next paragraph) as proceeding from below upward and from front to back This is in accord with our previous findings[1, 4]

(6) Since the first region of the entire septal mass to be activated is the middle one third of the left septal surface with the above in mind it now becomes possible to describe the sense of the general activation process of the interventricular septum This spread of activation vectorially considered is from left to right from below upward and from front to back Further proof of this has been vectorcardiographically demonstrated by Burchell *et al*[10] These authors working with Langendorff preparations of isolated canine septa have described an identical general process of septal activation

(7) In some cases in the high part of the septum we have found bilateral activation fronts proceeding from the right and left septal surfaces and converging at the mid line While these results are similar to those of Scher *et al*[1] it should be emphasized that this is seen in only some cases and in limited portions of the septum

The electrical partition of the septum We have long felt that the times of arrival of the activation process at various points within the septum cannot by themselves give indication as to which bundle and its ramifications are responsible for the activation of those points[4] It is absolutely necessary to investigate a point before and after bundle branch block has been produced In that way one can examine each point for change in morphology and time of activation If no change is noted that single point s activation then can be ascribed properly to the unaffected bundle

Some authors have produced extrasystoles in an attempt to simulate the conditions of bundle branch block There are several reasons why this technique is not entirely comparable to bundle branch block In the first place the complexes are different from those usually encountered in bundle branch block This difference is due to an aberrant spread of conduction The nature of the aberrant spread is as follows when we have produced extrasystoles in the interventricular septum (unpublished observations) the activation at first progresses very slowly giving a marked initial slurring to the recorded complexes Probably activation begins as muscular transmission causing the slow slur until the Purkinje system becomes activated In any case the complexes are markedly different from those encountered in bundle branch block Another point of considerable importance is that the timing of the premature beats within the cardiac cycle has not been controlled As a case in point premature excitation in the vicinity of the P wave can cause fusion beats The course of the spread of activation is markedly influenced by the state of excitability in the region and the surrounding area where the extrasystolic stimulus has been applied

We have proved that in at least the upper two thirds of the septum the bulk of the septal mass is activated through the left bundle Important also is the fact that there are regions of the right septal surface activated by the left

bundle The electrical mass of the right septum is only about one third to one fourth that of the left and its anatomical substrate is mostly trabecular tissue

In normal conditions these two electrical septal masses are functionally independent suggesting that we cannot consider the septal mass as a syncytium from the electrical point of view This idea was impressed upon us during our studies of left bundle branch block[3, 4] Under the conditions of block it took the activation process 0 02 sec to cross the boundary separating the right and left electrical components of the septum These observations of electrical independence have been confirmed by Maekawa and Ono[11] who have concluded In accord with Sodi Pallares it was found that functionally both left and right ventricles were independent with the index of electrical phenomena and did not make one simple syncytium

The anatomical partition of the septum In a dog s heart it is usually relatively easy to separate the right and left septal masses by blunt dissection F Bonetti and M Lev (personal communications) have studied this problem more extensively and have shown (1) that in normal human and dog hearts the left septal mass constitutes about 70 to 80 per cent of the total mass of the septum (this observation being for the upper two thirds) (2) that in the human heart showing left ventricular hypertrophy the left septal mass forms even more than 80 per cent of the total and (3) that in right ventricular hypertrophy the right septal mass may constitute 50 per cent or more of the eptal weight As we make no pretentions to being anatomists our imple findings in the dog s heart could be open to dispute but recently Lev (personal communication) gave us several excellent diagrams indicating the anatomical separability of the human septum into right and left ventricular masses Lev also points out that the ratio of septal masses right and left is similar to that of the right and left ventricular walls re pectively

QR and QRS complexes—the meaning of QR and QRS type complexes recorded in the upper parts of the septum and in both auricles As a corollary to our work in septal activation we have found predominantly QR and QRS complexes in unipolar records from the left and right superior portions of the septum Since the general sense of activation has been described as proceeding from below upward it might be anticipated that in such high leads an initial positivity should be recorded The production of the initial Q seen in these leads is due to the strong forces directed toward both apices and mid portions of the free ventricular walls overbalancing the component directed upward When the activation wave approaches the high recording electrode local forces dominate and a late R wave is inscribed In favor of this point of view is the previously cited work of Burchell *et al*[10] When these investigators took vectorcardiograms of the isolated heart the direction of activation was from above downward and the activation of the i olated septum was from below upward

Similar unipolar leads of the QR type have been de cribed by us as occurring within the cavities and on the epicardial surfaces of both the left and right auricle In another paper[1] it has been demonstrated that these auricular derivations reflect the potential variations occurring in the high left and right

septal surfaces This association has proven to be an extremely useful diagnostic tool in such conditions as atrial enlargement atrial defect and septal hypertrophy

Summary

No general agreement exists as to the process involved in the activation of the septum The following according to our experimental data represent the salient features of such activation

(1) The earliest site of septal activation is in the middle one third of the subendocardium of the left septal surface

(2) The most delayed sites are in the subendocardium of the posterosuperior portions of the septum The greatest delay is recorded on the right septum in this vicinity

(3) The general vector of septal activation is visualized as proceeding from left to right from below upward and from front to back

The correlation between the anatomical and electrical partition of the septum is discussed An analysis of the pitfalls in this type of experimentation is given

The complexes recorded from high septal areas are of the QR and QRS types The clinical implications are briefly discussed

References

1 Scher A M A C Young A L Malmgren & R V Erickson 1955 Activation of the interventricular septum Circulation 3 56
2 Durrer D L H van der Tweel S Berreklouw & L P van der Wey 1955 Spread of activation in the left ventricular wall of the dog IV Am Heart J 50 860
3 Sodi Pallares D M I Rodriguez L O Chait & R Zuckermann 1951 The activation of the interventricular septum Am Heart J 41 569
4 Sodi Pallares D A Bisteni G A Medrano & F Cisneros 1955 The activation of the free left ventricular wall in the dog s heart In normal conditions and in left bundle branch block Am Heart J 49 587
5 Scher A M A C Young A L Malmgren & R R Paton 1953 Spread of electrical activity through the wall of the ventricle Circulation Research 1 539
6 Sodi Pallares D E Barbato & A Delmar 1950 Relationship between the intrinsic deflection and epicardial activation Am Heart J 39 387
7 Sodi Pallares D New Bases of Electrocardiography C V Mosby St Louis Mo In press
8 Itatsu H 1954 Theoretical interpretation of contiguous bipolar ECG and its relationship of the time of arrival of activation Part I Fundamental studies Japan Circulation J 18 1
9 Cabrera E & D Sodi Pallares 1954 La activatión ventricular como fenómeno estadístico Arch inst cardiol Mex 24 448
10 Burchell H B H E Essex R D Pruitt 1952 Studies on the spread of excitation through the ventricular myocardium II The ventricular septum Circulation 6 161
11 Maekawa M & B Ono 1955 Experimental study of the electrocardiogram of the mammalian heart Japan Circulation J 19 110
12 Sodi Pallares D A Bisteni R G Herrmann 1953 Some views on the significance of the QR and QR type complexes in right precordial leads in the absence of myocardial infarction Am Heart J 43 716

THE CONDUCTING TISSUE AND CARDIAC ELECTROPHYSIOLOGY

By Jane S Robb
State University of New York College of Medicine Syracuse N Y

In experiments performed at the State University of New York College of Medicine stained sections of the hearts of several species have been shown to demonstrate the following

(1) Each of about 20 species studied[1] has a band of tissue situated on top of the muscular interventricular septum enclosed between the connective tissue layers at the lower edge of the membranous septum The staining reactions of this tissue are unlike those of cardiac muscle The conducting tissues stain more faintly with Masson or Mallory s trichrome or with silver stains Other studies have shown that surviving conducting tissue uses far less O_2 than surviving heart muscle[2] and also that the lipid fractionation of conducting tissue is unlike that of heart muscle (FIGURE 1)[3]

(2) Higher magnifications show many fine connective tissue septa dividing the bundle of His into numerous smaller tracts of varying diameters As one follows the tissue to the periphery these septa persist and even in subendocardial areas and in false tendons fluorescene staining and subsequent photog



FIGURE 1 Guinea pig heart One aortic cusp is seen on the right The cross section is of the main bundle with a branch penetrating the mid septum and joining the ventricular muscle end to end Other septal connections are on the right ×125



FIGURE 2 Human heart—silver stain Letter *B* indicates the bundle of His *LB* the left branch and *SB* the septal branch ×125

raphy demonstrate their presence The suggestion has been made that these tracts of varying diameter may conduct at variable rates similar to the variable conduction rates known to be true for nerve fibers of variable diameter

(3) The main bundle not only divides into right and left branches and gives off a branch high on the left (that is nearer the atrium) but numerous other branches penetrating the septal mass in its central portion and on the right also come from the main bundle (FIGURES 1 and 2)

(4) Nerves and blood vessels accompany these branches even those in the false tendons and in the free walls of the ventricles Note that the vascular distribution to the conducting strands is not from the same source that supplies the muscle to which it is distributed

(5) In all species the conducting tissue is ensheathed but only in ungulates is the surrounding space large enough to allow injection of particulate matter for example India ink or pigments (FIGURE 3)

(6) Peripheral distribution of the conducting tissue is three dimensional Moreover a given area of muscle may be supplied by more than one branch suggesting that if one track becomes damaged another may take over (FIGURE 4)



FIGURE 3 India ink injection of the conducting tissue sheath in the beef heart—lateral wall left ventricle The endocardium is at the left Note the complexity of the pathways and the distribution in numerous planes ×1 0

(7) It has been postulated that if the conducting or specialized tissue truly has the function of being the pathway over which the wave of depolarization passes from the atrioventricular (AV) node to the ventricular muscle then a relationship must exist between its distribution and the pattern of ventricular activation The analysis of this relationship is complicated by (a) the three dimensional distribution (FIGURE 3) (b) overlapping distribution of some branches (FIGURE 4) (c) variable diameter of tracts within the system suggesting variable rates of conduction and (d) the inevitability of injury to one or many paths whenever a penetrating electrode is positioned (FIGURE 3) For example records taken by penetrating electrodes (multiple channel pattern) have shown repeatedly that the subendocardial tissue is activated first and that subepicardial areas are activated later It does not follow however that one can measure the distance between the openings on the electrode and calculate the conduction rate within the muscular wall because no one can tell whether some direct pathway is aligned with the electrode or has been damaged or if so what is the length of the bypass It is possible that the areas at the bases of the ventricles known to be activated last may be supplied by small branches leaving the main bundle but conducting slowly The apical region and the trabeculated area receive the larger branches and are known to

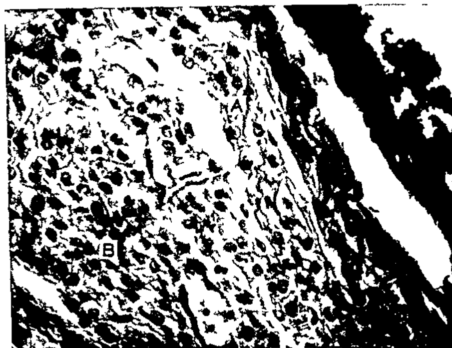


FIGURE 4 Higher magnification to demonstrate the transition of the conducting tissue tract (*A*) and of a second tract immediately to the right of *A* to ventricular muscle (the dark tissue at the lower edge) Area *B* is also ventricular muscle ×500

be activated early It may be that these larger branches conduct much more rapidly One may question whether the *entire* sinus node, acting as pace maker fires simultaneously and even whether the entire *AV* node is activated at one instant One may postulate that an area in the pacemaker activated late may eventually activate an area in the *AV* node that also fires late and that thence the excitation may pass by narrow diameter pathways to the areas of the ventricle that are activated last

References

1 BAIRD J A & J S ROBB 1950 Anat Record 108 747
2 MURRAY J B 1954 Am J Physiol 177 463
3 MALLOV S J M MCKIBBIN & J S ROBB 1953 J Biol Chem 201 825

DISCUSSION PART II

Howard B Burchell *Chairman*

A M SCHER (*University of Washington Seattle, Wash*) I should like to comment on the use of bipolar leads A large interelectrode distance in bipolar leads produces one type of record while a reduction of the distance by moving the two electrodes together produces another In such leads one portion of a rapid deflection does not have a greater interpretive significance than another The final configuration is to a large extent a matter of technique

In our studies on septal excitation our electrodes were inserted into the septum from the right side and were advanced toward the left In normal conduction we always obtained a reversal of polarity of the deflections in the center of the septum Our sign of bundle branch block was a failure to obtain such a reversal In this respect our results differ from those of others

E FRANK (*University of Pennsylvania Philadelphia, Pa*) Anyone who has made electrical measurements knows that the values to be measured can be influenced by the method of measurement I should like to ask what experimental evidence if any is available to prove the validity of the data that have been presented Is the voltage to be measured not influenced by the introduction of the electrodes? Recording simultaneous control leads does not necessarily answer the problem

A SCHER Young and I were careful repeatedly to record a standard lead II as a control before the insertion of the probe electrodes As we inserted the electrodes lead II was constantly monitored and was found to remain unchanged I should think this is as close as one can come to answering Frank s question

M PRINZMETAL (*Cedars of Lebanon Hospital Los Angeles Calif*) My associates and I have worried about the same question Frank has asked it is a very difficult question to answer The experiment that seemed to us to indicate that the intramural recording technique was a valid one was designed as follows One electrode was placed over the epicardial surface and another was placed within the ventricular cavity Unipolar records were taken with each search electrode as an exploring contact Then we placed a needle electrode directly underneath the epicardial and another directly over the endocardial contacts If the presence of the needle electrode were to cause significant changes marked alterations in the configuration of the recorded complexes from the epicardial and from the endocardial surfaces should occur With the needle electrodes in place however there was practically no change in any of the surface leads (epicardial or endocardial)

D SODI PALLARES (*The National Heart Institute Mexico D F Mexico*) The hypothesis of the instantaneous spread is very interesting to me By calling the conduction rate infinite we are merely emphasizing one inherently difficult aspect of the problem What my associates and I along with Jane Robb, wish to say is that simultaneous activation of various points may occur, were our electrodes inserted at these points we should determine the velocity of activation as a finite distance divided by zero (time) and the result would

become infinity It is dangerous to speak of the spread of activation when the problem is so viewed E Cabrera who has done very excellent work on this problem offers the following interesting hypothesis which accords with the observable facts Simultaneous activation of many subendocardial points would create many small foci of activation each expanding radially These small globes would contain an inner layer of negativity surrounded by a shell of positivity of the same charge density By the Gauss theorem, recording points within these small islands of activation would record negativity while points without (such as precordial or epicardial leads) would give zero potential With coalescense of these spheres of activity into a defined wave front increasing R waves would begin to be recorded at the epicardium and S waves would begin to be recorded within the cavity For this reason we have begun to denote two kinds of endocardium (1) the anatomical endocardium and (2) the electrical endocardium

H H Hecht (*University of Utah Salt Lake City Utah*) May not the variable results reported for the spread of ventricular excitation depend to some extent on the considerable differences in the development of the bundle of His in various species? I remember a series of experiments that Wilson and I carried out with Alfredson of the Agricultural College in Lansing Michigan[1] Alfredson had tried unsuccessfully to induce bundle branch block in calves by cutting either side of the septum He doubted the accuracy of his own technique and had asked Wilson to try his luck We were equally unsuccessful in our efforts to produce bundle branch block although as was later seen the cuts had been properly placed and complete atrioventricular block had occurred when both sides of the interventricular septum had been cut The inference of course is that because of the very well developed conduction system in cattle and in ungulates in general conduction was accomplished without difficulties from the contralateral side via the ramification of an excessive Purkinje system As I said it seems to me that some of the discrepancies may result from the unequal extent to which the conduction system is developed perhaps from animal to animal and certainly from species to species

Reference

1 Alfredson B D & J F Sykes 1940 Studies on bovine electrocardiogram II Bundle branch block Proc Soc Exptl Biol Med 43 580

E Lepeschkin (*University of Vermont Burlington Vt*) I should first like to call attention to figure 1 sent to me from Brazil by Ennio Barbato who has made extensive studies of surface depolarization in the human heart during thoracic operations Figure 1 is one of the cases in which a large number of points have been studied Barbato found that in the majority of cases the first to be activated are the right paraseptal regions followed more or less simultaneously by the apex of the right ventricle the intermediate zone some points of the pulmonary conus the left paraseptal regions the apex of the left ventricle and finally by the intermediate and basal regions of the anterior and lateral surfaces The diaphragmatic surface has not been studied

Another problem worthy of consideration is the thickness of the ventricular wall related to the time of appearance of the excitation on the surface. I do not think systematic studies on this are too numerous. I have just read a paper by Busch[1] of Vienna, who has measured the thickness of different parts of the ventricles in a large number of cases. Calculating the average values for normal hearts from his tables I found the average thickness in millimeters at the apex of the right ventricle to be 1, at the base anteriorly 1.7 and at the base posteriorly 2.6. The thickness at the apex of the left ventricle was 3.9 and at the base of the left ventricle the same average of 6.3 was found posteriorly and anteriorly. You can see that the ventricular wall is thinnest where in general the excitation appears first on the surface.

Another interesting point is that the wide QRS of ventricular extrasystoles seems to indicate that here the activation of the myocardium proceeds entirely

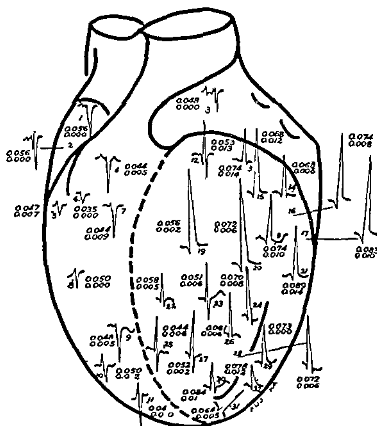


FIGURE 1. Direct unipolar leads taken from different points on the surface of the heart previous to a lobectomy in a 43 year old male with an abscess of the lower left pulmonic lobe. Each point is numbered and a facsimile of the corresponding electrocardiogram is drawn at or near each point. The first number near each drawing indicates the end of the intrinsic deflection in relation to the beginning of QRS in a synchronous limb lead. The second number indicates the interval between the first ventricular deflection in direct leads and that in the indirect leads (courtesy of Ennio Barbato, São Paulo, Brazil).

over nonspecific musculature without involving the conducting system I wonder why this is the case If the Purkinje system is so widespread in the heart one might expect the excitation to enter very rapidly and once that has happened the excitation of the remaining parts of the heart would be as rapid as in normal beats I think one of the explanations is that the Purkinje system has a very large cell diameter while the diameter of the myocardial fibers is small so that the conducting system can develop sufficient current to excite the nonspecific muscle fibers However the regular muscle fibers because of their high resistance may not develop enough current to excite the conducting system I think this is partly why retrograde conduction into the atria occurs so rarely in ventricular extrasystoles To be sure if the extrasystoles are early the failure to enter the conducting system can be attributed to the greater duration of the refractory phase in the latter

In closing I should like to say that the direction of the muscle fibers is related to the direction of the excitation The anastomoses between the myocardial fibers take place in a longitudinal direction so that conduction across the fibers must take place along a zigzag path Pruitt *et al*[2] have shown that in excised strips from the muscle surface the conduction velocity is much faster in the direction of the fibers than it is perpendicular to their direction

Another point is that regardless of the sequence of activation the potentials occurring during the process of excitation are directed along the long axis of the muscle fibers This corresponds to Schaefer s observation that the highest voltage is observed when the bipolar electrode is parallel to the muscle fibers

H B Burchell The work to which Lepeschkin refers is that of Pruitt and Essex and myself We are sure of what we saw, but we are not quite so sure as Lepeschkin of our interpretation Nevertheless the results stand, to be interpreted by others

References

1 Busch W 1955 Neue Ergebnisse der Messung und Wagung der Herzkammern bei den verschiedenen Hypertrophieformen mit besonderer Berücksichtigung der Histologie Arch Kreislaufforsch 22 267
2 Pruitt R D H E Essex & H B Burchell 1951 Studies on the spread of excitation through the ventricular myocardium Circulation 3 418

TABLE I

CASE F C 32 YEAR OLD HOUSEWIFE ATTACKS OF RAPID HEART ACTION (FIGURES 1 AND 2)

	Normal complexes (sec)	Abnormal complexes (sec)
PR interval	0 156	0 080
QRS interval	0 068	0 132
QT interval	0 348	0 352
P R peak	0 180	0 176
P S peak	0 220	0 220
A_{QRS}	32 6	99 8
A_T	32 4	−27 4
G	69 2	69 2
α_F QRS	78	76
α_F T	76	−109
α_F G	77	77

Magnitude of frontal plane vectors in microvolt seconds
$\alpha_F = \alpha$ as projected on the frontal plane

stances it seems possible that the entire ventricular mass responds to premature excitation[8]

(2) The condition is unstable to the extent that if it does not occur spontaneously it is almost always possible by a variety of procedures to induce a normal atrioventricular conduction with normal QRS configuration Wolff[9] has summarized the various procedures that have been employed for this purpose As an example powerful vagal stimulation will normalize the anomalous QRS complexes by paralyzing the sinus node and shifting the pacemaker into the lower atrial region the AV node or the common branch of the His bundle The transient hypertension with reflex cardiac slowing induced by 1 mg (0 1 ml) of Neo-synephrine hydrochloride given intravenously appears particularly effective (FIGURES 3 and 4) To be able to demonstrate the coexistence of normal pathways is often desirable It may dispel the notion that the syndrome is some form of an intraventricular conduction defect (a common interpretive error) or it may unmask such changes in ventricular excitation as ventricular enlargement and myocardial infarction that are present simultaneously but are not readily apparent during the anomalous excitation[7, 10]

THE CLINICAL ENTITY OF THE SYNDROME

L WOLFF (*Beth Israel Hospital Boston Mass*) In 1928 a vigorous young athlete was referred to Paul D White s laboratory because his physician was perplexed by the occurrence of paroxysmal atrial fibrillation in a healthy individual History physical examination and X ray failed to reveal any evidence of heart disease except for episodes of rapid heart action The electrocardiogram disclosed abnormal ventricular complexes and the PR interval was 0 10 sec Since paroxysmal tachycardia had occasionally occurred during a workout in the gym he was requested to run up and down four flights of stairs in the hope of provoking an attack The effect of exercise was unexpected the ventricular complex became normal and the PR interval increased to 0 16 sec although the heart rate rose to levels of 120 to 140

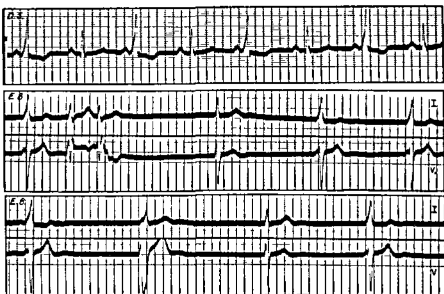


FIGURE 3. Alternating anomalous atrioventricular excitation (D. S.) and forced normalization (F. B.). D. S. is an example of a spontaneous alternation of anomalous excitation with delta waves (beats 1, 3, 5 and 7) and normal conduction (beats 2, 4, 6 and 8). E. B. is an example of anomalous atrioventricular excitation 35 sec. after the intravenous injection of 1 mg. of Neo-synephrine hydrochloride. In the middle row beats 1, 5 and 6 are of the anomalous variety and beat 4 is a normal complex (beats 2 and 3 are left ventricular extrasystoles). In the lower curve beats 1 and 4 are anomalous, beat 3 is normal, and beat 2 represents an accentuated anomalous beat apparently caused by the response of an unusually large area of ventricular muscle to pre-excitation (concertina effect of Öhnell). The time lines are 0.1 sec.

The anomalous type of electrocardiogram was again observed on the young man's next visit to the laboratory and this time the subcutaneous injection of atropine had the same effect as had exercise during the preceding visit.

In the ensuing weeks it was possible to reproduce these changes at will. On one occasion the control electrocardiogram was normal and carotid sinus massage was followed at once by prolongation of the QRS interval and abbreviation of AV conduction time.

The electrocardiographic files were searched and six similar cases were found. This meager material was studied with great care and happily the conclusion was reached that the abnormal ventricular complex, the short PR interval and the paroxysmal tachycardia had a common basis. The brevity of the PR interval was significant only if the cardiac pacemaker was in the SA node, a fact that our preliminary observations established beyond any doubt.

Many questions required consideration, some of which are still unanswered today, such as the nature of the mechanism responsible for the peculiar electrocardiogram, the mechanism of the paroxysmal tachycardia and the etiology of the syndrome and its clinical significance. It seemed to us then and it still

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does today that the condition is congenital, its occurrence in newborn and premature infants supports this contention I have seen five cases in a single family occurring in a parent and his children indicating that the syndrome may be hereditary and familial The evidence concerning acquired anomalous conduction is incomplete and at best equivocal In keeping with the congenital nature of the disorder is its occasional association with congenital heart disease of the ordinary types and of special significance is its frequent association with Ebstein s anomaly Nevertheless the vast majority of patients with this syndrome have no demonstrable independent heart disease nor do they coincidentally acquire recognized varieties of heart disease

There are no subjective manifestations or hemodynamic derangements associated with anomalous atrioventricular excitation per se Normal activity is enjoyed by most patients and longevity is achieved by some The severity of paroxysmal tachycardia may however be incapacitating and because of the uncertainties engendered by rapid heart action, occupations in which faintness diminished mental alertness and loss of consciousness might result in unusual hazards must be prohibited In spite of the generally benign course of the disorder sudden unexpected death does occur and life insurance experience indicates that applicants with the WPW syndrome are not standard risks in that their mortality rate is approximately three times normal

The mechanism responsible for the abnormal electrocardiogram aroused our interest in 1928 and although the idea of a muscular bypass occurred to us it seemed fanciful and unsupported by the facts available We turned to the literature for help but found none It so happened that White had started out on a visit of foreign medical centers at this time and he had taken with him the electrocardiograms that were our great concern The reaction to them in two cities is worth recording In Vienna the opinion was expressed that the tracings did not represent anything more unusual than bundle branch block and AV nodal rhythm In London Sir John Parkinson s interest was aroused and he offered to look through his files in the hope of finding similar cases He found three or four and graciously sent the material to us for incorporation in our paper[2]

The widespread interest that followed publication of the first paper in 1930 centered chiefly around the mechanism responsible for the abnormal electrocardiogram It became a matter of considerable importance to know whether an explanation within the framework of current knowledge of cardiac physiology was adequate or whether new concepts were needed for this purpose It is generally agreed that premature activation of a fraction of ventricular musculature is responsible for both the short PR interval and the abnormally wide QRS complex but there is considerable difference of opinion concerning the manner in which it is brought about These opinions embrace two concepts the one supposes the mechanism to be an anomaly of impulse formation the other assumes that it is an anomaly of conduction Both concepts are adequate to account for the high incidence of paroxysmal tachycardia which occurs in about 75 per cent of all patients displaying the type of electrocardiogram under discussion

Experimental production in animals and in man of electrocardiograms simi

lar to those seen in patients with the WPW syndrome have stimulated hopes of solving the riddle of the abnormal tracing Some of these experiments however are difficult to understand and the electrocardiograms are subject to varied interpretations It seems that we have lost sight of the real problem in our zealous effort to elucidate the disorder If we limit the possibilities to the concept of anomalous excitation it would appear that a muscular bypass is significant only if it provides a through pathway from the atria to the ventricles without participation by any part of the normal AV connections The location of such a viaduct is of only secondary importance even if it lies buried within the AV node so long as it is anatomically and physiologically independent of the latter structure In traversing such a pathway the impulse is not subjected to physiological delay in the AV node and it thus reaches the lower chambers in accelerated fashion There is considerable evidence for the complete muscular bypass and this mechanism explains all known phenomena of the syndrome without invoking new concepts This is quite different from the mechanism that is envisaged by accelerated conduction a quickening of conduction in the tissues of the normal AV pathway This embraces a concept that is unproved although it is capable of explaining some features of the syndrome

In summary the WPW syndrome is of interest from a clinical point of view but especially in respect to its bearing on the cardiac mechanism The weight of evidence supports the mechanism of the muscular bypass a concept that lies within the framework of current knowledge

Electrocardiographic Analysis

F F Rosenbaum (*Marquette University School of Medicine Milwaukee Wis*) The term anomalous atrioventricular excitation is not one for which I

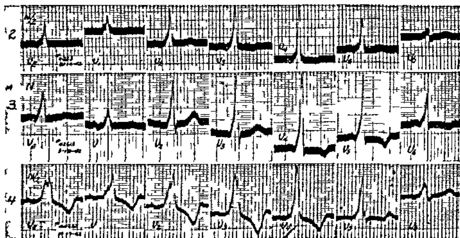


Figure 5 Precordial leads in 3 patients with anomalous atrioventricular excitation Type A (figure 6 from Rosenbaum *et al* [4])

take any credit Wilson made the original suggestion that this disorder be designated anomalous atrioventricular conduction However even at that time there was considerable uncertainty that we were dealing with an actual muscular bypass and I suggested that the term excitation was more inclusive than the word conduction Wilson agreed to this minor change in terminology Upon whatever mechanism of anomalous atrioventricular excitation there is ultimate agreement it must be one that is compatible with a large body of facts including a number of unusual electrocardiographic features other than the short PR interval and the broad QRS complex

On the basis of the configuration of the usual precordial leads these cases have been divided into types A and B FIGURE 5 shows the precordial electrocardiograms of three patients with this disorder all of them falling into type A In all of these records it is clear that the delta wave or pre excitation component is positive The initial slow upward slurring of the R wave so characteristic of the electrocardiograms in the WPW syndrome is shown very well over the entire precordium in these cases

In type B illustrated in the lower 2 tracings in FIGURE 6 the delta wave or pre excitation component is negative or if positive at least very small in the records taken from the extreme right precordium In some instances as shown in the upper 2 sets of tracings in FIGURE 6 there seems to be something of an admixture of types A and B Although the separation of these 2

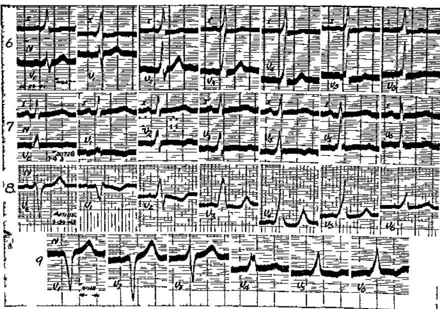


FIGURE 6 Precordial leads in 4 patients with anomalous atrioventricular excitation Cases 8 and 9 are type B Cases 6 and 7 are intermediate between types A and B (figure 11 from Rosenbaum *et al*)

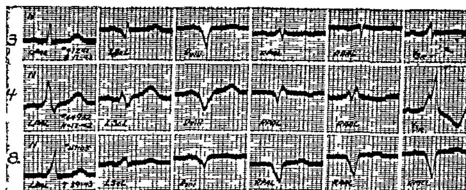


FIGURE 7 Posterior thoracic leads in 3 patients with anomalous atrioventricular excitation (figure 7 from Rosenbaum *et al*)

types of cases into these categories may well be largely arbitrary and artificial these different configurations are quite probably related intimately to the area of initial excitation or pre excitation of the ventricle and are due at least in part to differences in the order of ventricular excitation

In general it may be said that in anomalous atrioventricular excitation the dorsal aspects of the ventricle appear to be activated prematurely In FIGURE 7 the circum thoracic leads in three patients with this disorder are illustrated These leads have been recorded in a number of patients, and it appears that in most instances all parts of the thorax except a zone of small to moderate size usually located posteriorly show a significantly large initial positive de flection This latter zone is variable in its location and breadth from case to case In cases 3 and 4 in FIGURE 7 it is located in the left scapular line or at the eighth dorsal spinous process and is quite narrow In case 8 in FIGURE 7 and in the example shown in FIGURE 8 the zone of initial negativity is much broader and extends from the eighth dorsal spine to the right midclavicular line

Leads from the auricular level of the esophagus (E_{24} and E_{27} of FIGURE 9) in patients with anomalous atrioventricular excitation usually show large QS deflections and extremely short PR intervals often measuring only 0 05 or 0 06 sec These features suggest that the exploring electrode is very near to the site of initial activation of the ventricle It is of interest that in this par ticular patient (FIGURE 9) the electrocardiograms recorded from the esophagus at levels above the auricle (E_{15} and E_{18}) are practically the reciprocal of records made at the ventricular level of the esophagus (E_{42} E_{45} and E_{51})

One of the most interesting features of at least a few of these patients has been the variability of the thoracic electrocardiogram in the same patient from one observation to another Two and possibly three different precordial elec trocardiographic patterns were recorded on one patient on three separate occasions over a period of two and one half years (FIGURE 10) These precor dial electrocardiograms were recorded from the same points over the thorax on the same woman on March 5 1941 November 3 1941 and December 31

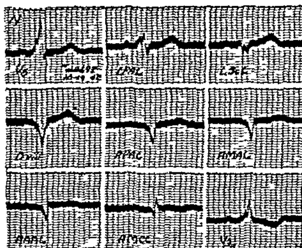


FIGURE 8 Records from the left axilla the back the right axilla and the right anterior thorax in a patient with anomalous atrioventricular excitation (figure 4 from Rosenbaum *et al*)

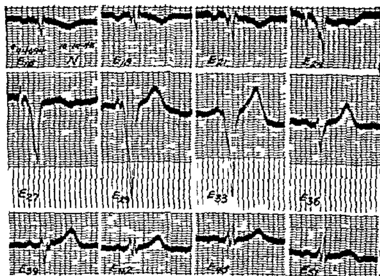


FIGURE 9 Esophageal leads from a patient with *anomalous atrioventricular excitation* (same patient as in FIGURE 8) *The* subscript indicates the distance in centimeters of the exploring electrode from the nares (figure 3 from Rosenbaum *et al*)

1943 It will be seen that the original record fall into type B whereas the final tracings fall into type A and the third record falls into something of an intermediate category Observations such as this suggest that in some patients there may be more than a single anomalous pathway or more than a single anomalous operating mechanism

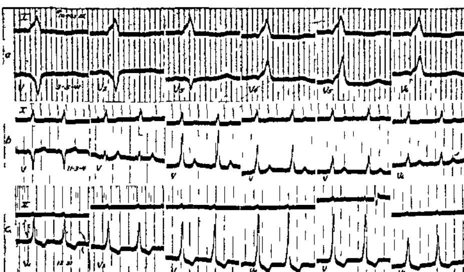


FIGURE 10 Three sets of precordial leads recorded on 3 separate occasions on the same patient (simultaneous limb lead on each occasion) Note the variation in the form of the ventricular complexes of the precordial leads (figure 14 from Rosenbaum *et al* [4])

It seems proper to point out here that the electrocardiographic manifestations of myocardial infarction may or may not be obscured by anomalous atrioventricular excitation Wolff and Richman have published an important communication dealing with this matter [10] The patient whose electrocardiograms are shown in FIGURE 11 had a posterior myocardial infarction in addition to anomalous atrioventricular excitation The diagnosis and localization of the infarction were confirmed by post mortem examination In this instance the usual features of posterior infarction are seen in leads II III and V_F However in some published examples of myocardial infarction and anomalous atrioventricular excitation this has not been true particularly with anterior infarction It seems very probable that the anomalous spread of the activation wave through the ventricle particularly with late activation of the anterior aspects of the left ventricle is responsible for obscuring the electrocardiographic signs of infarction This represents another electrocardiographic facet of this disorder that must be fitted into our ultimate understanding of this anomaly

The anomalous mode of activation seems sometimes to persist in these patients during paroxysmal tachycardia or paroxysmal auricular fibrillation An example of this is shown in FIGURE 12 occurring in a man who was the son of the patient whose electrocardiograms are shown in FIGURE 11 These records were made during a paroxysm of rapid heart action that persisted over a period of at least six days The ventricular complexes recorded during the paroxysm are essentially the same in outline as those that had been recorded several years earlier and were recorded shortly after the termination of the attack (FIGURE 12 4 10-45) This patient died suddenly two hours after conversion to normal rhythm occurred Langendorf Lev and Pick[11] have indicated that

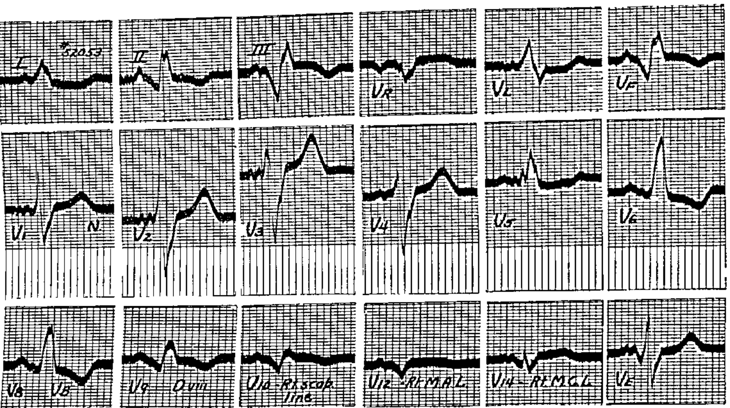


FIGURE 11 Anomalous atrioventricular excitation and posterior myocardial infarction

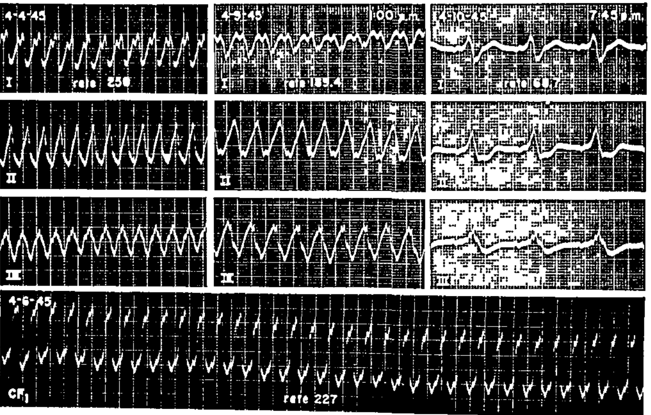


FIGURE 12 Paroxysmal supraventricular tachycardia in anomalous atrioventricular excitation with the persistence of the anomalous mechanism The precordial leads on the same patient recorded 3 years earlier are shown in FIGURE 5 case 4 The patient was the son of a man whose records are shown in FIGURE 10 (Rosenbaum F F R S Ballmer and F N Wilson Unpublished)

the examples of WPW syndrome with paroxysmal ventricular tachycardia that have been recorded in the literature are in many cases erroneously interpreted instances of auricular fibrillation with anomalous atrioventricular excitation in which the anomalous mechanism has persisted during the rapid heart action When a rapid regular ventricular rate with bizarre complexes is encountered careful interpretation is necessary before the diagnosis of paroxysmal ventricular tachycardia can be made especially if the ventricular complexes are similar to those recorded during normal sinus rhythm because some of these cases are in truth instances of paroxysmal supraventricular tachycardia with persistence of anomalous conduction [11]

The demonstration of atrioventricular block associated with anomalous atrioventricular excitation is one of the most significant factors in the understanding of this disorder Although the actual number of such cases reported has been small these are well documented and various degrees of atrioventricular block have been observed Among these reports have been those of Scherf Blumenfeld and Mueller [6] Levine and Burge [12] and Pick and Katz [13] The electrocardiograms shown in FIGURE 13 were recorded from the same patient whose tracings are illustrated in FIGURE 12 Low grade partial heart block is seen to be present during supraventricular tachycardia with a persistence of ventricular complexes of anomalous form Slight variations in cycle length account for the minor differences in the RR intervals recorded from beat to beat Very occasional ventricular extrasystoles were also recorded Actually according to some of the hypotheses advanced atrioventricular block should not occur in this disorder if the impulse is blocked in its passage through the anomalous pathway it should travel down the normal path at the normal rate If the impulse is blocked in its passage down the normal pathway it should travel down the anomalous pathway with pre excitation of an even greater than usual share of the ventricular musculature For similar reasons if there is no actual muscular or structural bypass block should not occur It is difficult to conceive of a situation in which both an anomalous pathway and the normal conduction pathway from the auricle to the ventricle are completely blocked at exactly the same instant Block might occur however if the anomalous pathway had its origin in the very lowest portions of the atrioventricular node or just below it but above the division of the bundle of His into its major branches Situations such as that recorded in FIGURE 13 might also be explained if one were to assume that ventricular activation in this patient was dependent entirely upon an anomalous pathway and that conduction over the normal pathway never occurred Cases of WPW syndrome with partial or complete heart block of some degree would seem to argue rather strongly against any mechanical or electrotonic type of pre excitation of a portion of the ventricle by auricular activation or by contraction because here again if pre excitation does not occur normal conduction should result On this particular point Wilson *et al* wrote Observations pointing clearly to the presence of partial block in the accessory pathway would greatly strengthen the view that the anomaly is structural [4]

There have been several reports of histological studies supporting the belief

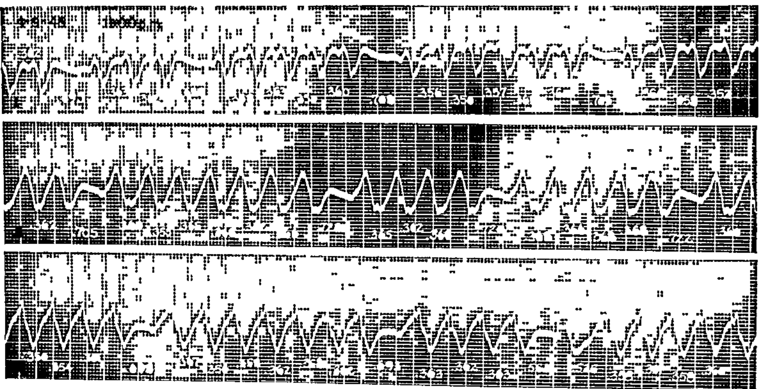


FIGURE 13 Paroxysmal supraventricular tachycardia with low grade partial atrioventricular heart block and persistence of the anomalous mechanism Same patient as in FIGURE 12

that there is a structural anomaly that corresponds to the electrocardiographic features of this disorder The recent study of Lev Gibson and Miller[14] is concerned with observations of over 12 000 sections from the heart of a child with Ebstein s disease and anomalous atrioventricular excitation In this heart there was an intermediary bundle in the connective tissue of the atrioventricular groove that gave off fasciculae to the right atrium and right ventricle a small high communication between the right bundle branch and the ventricular septal wall on the right and an encasement of fibroelastic tissue around the right bundle branch These observers also reported that they did not find such communications in an appreciable number of normal infants and children whose hearts were examined with the same technique Wood Wolferth and Geckeler[15] found three communications between the right auricle and the right ventricle in a case they studied Öhnell[7] reported a communication between the left auricle and the subepicardium of the left ventricle dorsal to the mitral orifice and about 4 cm from the ventricular septum Levine and Burge[3] found a band in the right posterolateral aspects of the heart bridging the atrioventricular groove continuous with the ventricular muscle and penetrating deep into the auricular muscle Kimball and Burch[16] studied one case in which connections between both the right auricle and ventricle and the left auricle and ventricle were present One of the difficulties in the evaluation of the histological observations that bear upon this problem has been the wide variation in techniques employed by the different observers

FURTHER OBSERVATIONS ON THE SPREAD OF VENTRICULAR EXCITATION

H H HECHT In spite of the voluminous literature little information concerning the details of the electrocardiographic configuration has been added during the last ten years to supplement Rosenbaum s analyses The use of endocardial leads and the combined use of esophageal endocardial and precordial leads that we have carried out on fourteen additional cases[17] have tended to consolidate further the electrocardiographic aspects Similar studies have been reported by Sodi Pallares and his group[18] who have confirmed the classification we proposed[4] and by Grishman Kroop and Steinberg[19] who doubted that a division into separate groups was feasible or necessary

Rosenbaum mentioned the early onset of ventricular depolarization in high esophageal leads that may indicate that regions of pre excitation have a tendency to be located posteriorly and basally This may be supported by an endocardial pull through of the kind illustrated in FIGURE 14 The record begins with the catheter within the right ventricular outflow tract Pre excitation contributes little or nothing to the endocardial tracing that begins after the end of the delta waves in a simultaneously recorded lead I As the catheter is withdrawn the width of the endocardial QRS increases steadily until it reaches almost twice the width of the QRS obtained at another position within the same cavity The onset of premature ventricular excitation in the endocardial electrocardiogram now begins during a period still occupied by the P wave in lead I Indeed the region of early excitation must be located close to the upper portion of the ventricular septum near the tricuspid valve Since QRS complexes within the ventricular cavity are of the normal configuration

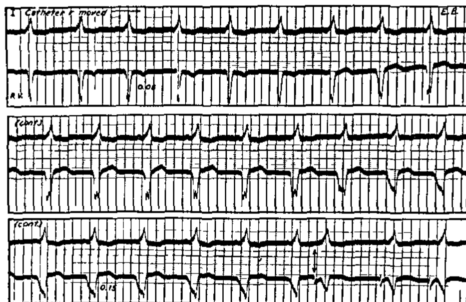


FIGURE 14 Endocardial pull through in anomalous atrioventricular excitation Note the inverted T waves of the normal endocardial complexes changing to upright complexes with an increase in the QRS area (secondary T wave changes) The arrow indicates the transition from the right ventricle to the right atrium The time lines are 0 1 sec

(although lacking a mall R that is commonly present) in spite of the very premature onset of excitation one can further argue that a region on the right side close to or within the base of the septum was responsible for the pre excitation and that the remainder of the ventricular musculature was excited over normal pathways This is the pattern obtained from type B of the syn drome Type A characterized by upright QRS groups in all precordial leads shows some of the characteristics of right bundle branch block in the endo cardial leads indicating that excitation of the right ventricle follows that of the left and that the endocardial electrode faces the advancing depolarization process Type A therefore is compatible with advance excitation of basilar septal areas of the left ventricle and type B is compatible with that from the right side (FIGURE 15)

Further confirmation has come from simultaneously recorded esophageal leads If the direction of pre excitation were in general more from right to left in type B lower esophageal leads should show slurred upright components of R (delta waves) if it were predominantly from left to right in type A a small R or a deep QS deflection would be expected This is clearly demon strated in FIGURE 16 E ophageal leads from regions below the atria are perhaps of greater value than atrial esophageal leads that may show only early excitation with extremely short PR segments It should be recalled that the peak of esophageal P waves in any case is considerably later than that

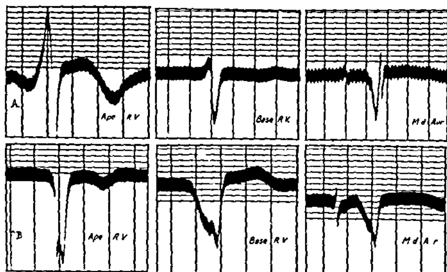


FIGURE 15 Endocardial complexes in anomalous atrioventricular excitation. The upper record is type A with late excitation of the right ventricular cavity. The lower record is type B with early normal (apex) and premature excitation (base) of the right ventricular cavity. Similar findings have been reported by Sodi Pallares and his co-workers.[18] The time lines are 0.1 sec.

of standard and precordial leads and that the PR is apparently shorter because of the late activation of the left atrial musculature.[20]

Information of this type tends to confirm the concepts laid down by Wolff and by Rosenbaum. I believe that a subclassification into two types serves a descriptive purpose by indicating in a general way the orientation of the excitation of the ventricular musculature, although variations and mixtures do occur. Further delineation[7] appears unwarranted and may introduce an element of confusion. On the other hand, it is difficult to deny that these two main types exist. A detailed report[19] employing essentially similar techniques has failed to confirm such differences—perhaps because only one type of the anomaly was studied.

It was to be expected that the vectorcardiographic analysis would show a rather slow traversing QRS loop from right to left on the frontal plane and, depending on the type, a more or less striking anterior displacement in the horizontal and sagittal planes. Several vectorcardiographic analyses are now available.[21, 22]

THE VECTORCARDIOGRAM IN ANOMALOUS ATRIOVENTRICULAR EXCITATION

I. WOLFF. The vectorcardiograms reproduced in FIGURES 17 to 20 were obtained from patients with the WPW syndrome using the double cube reference system of Duchosal with positive polarity. Patients exemplifying a wide age range and cardiac status were chosen (TABLE 2). The initial forces

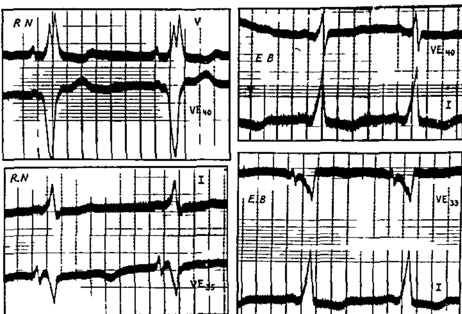


FIGURE 16 Simultaneous precordial and esophageal leads in anomalous atrioventricular excitation In R N (type A) the lower esophageal leads (representing the left ventricular cavity) show QS deflection The cavity leads show RS type complexes (FIGURE 15) and the right sided precordial leads show very late R peaks This suggests pre excitation of the ventricular muscle from left to right In E B (type B) the lower esophageal leads show RS type complexes and QS deflections are present inside the right ventricle (FIGURE 15) and over the right precordium Higher esophageal leads also show QS deflections indicating that the leads from this region do not represent left ventricular cavity effects Pre excitation should occur from right to left in this type

TABLE 2

INITIAL AND TERMINAL FORCES AND CLINICAL DIAGNOSIS IN PATIENTS WITH THE WOLFF PARKINSON WHITE SYNDROME

Case No	Age	Initial force	Terminal force	Type ‡	Clinical diagnosis
I	5	LPD	LPU	B	? Congenital heart disease slight cardiomegaly
II	55	LPU (LPD)	LPU (LPU)	B	Anterior myocardial infarction
III	58	LPU	LPU	B	Normal heart
IV	78	LOU (RPU)†	RAU (RAU)†	A	Anterior posterior and septal myocardial infarction (confirmed at autopsy) right bundle branch block

Symbols L = left P = posterior D = inferior U = superior O = no anterior or posterior displacement

Normal intraventricular conduction

† Right bundle branch block

‡ See Rosenbaum *et al*



FIGURE 17 Vectorcardiogram in a 5 year old girl with possible congenital heart disease and slight cardiomegaly In all the figures the arrows indicate the direction of the inscription of the QRS loop and the interruptions equal 0 0025 sec H is the horizontal plane projection S the sagittal plane and F the frontal plane In relation to the patient the bottom of the figure is anterior (H) or inferior (S and F) and the top of the figure is posterior (H) or superior (S and F) The observer's left corresponds to the right (H and F) or posterior (S) and the observer's right corresponds to the left (H and F) or anterior (S) in relation to the patient The initial and terminal forces are given in TABLE 2 The record is presumably type B and it may be influenced by the presence of ventricular enlargement

which correspond to the anomalous component of the QRS complex or delta wave of the electrocardiogram are remarkably similar in all the patients The presence of infarction in the anterior and posterior walls of the left ventricle and of the intraventricular septum (FIGURE 17) apparently did not interfere with the mechanism in the cases studied

The presence of right bundle branch block in case 4 (TABLE 2 and FIGURE 19) likewise did not interfere with the anomalous mechanism evidently excluding the right bundle branch as the anomalous pathway The left bundle branch can also be separated from the anomalous pathway as indicated by the striking change in the spatial orientation of initial forces when anomalous excitation disappears since the initial forces in FIGURE 19 must represent depolarization of the ventricular myocardium via the left bundle branch

There appears to be a relationship between the terminal forces and the type of electrocardiogram as defined by Rosenbaum *et al* [4] This is further suggested by the similarity of the initial forces in both types (TABLE 2) We reach the tentative conclusion then that the type classification does not depend at least directly on the anomalous pathway or that the differences are not apparent in vectorcardiograms with low resolving power

FUSION BEATS AND ANOMALOUS ATRIOVENTRICULAR EXCITATION

D SODI PALLARES (*The National Heart Institute, Mexico D F Mexico*) I am impressed with the relative frequency with which the WPW syndrome appears during the administration of anesthesia preliminary to surgery Certainly the aberrant pathway cannot be formed during this acute procedure If a latent pathway awaited the anesthetic agent to call it into play then we are forced to postulate that aberrant pathways are very common This supposition does not accord with current anatomical knowledge

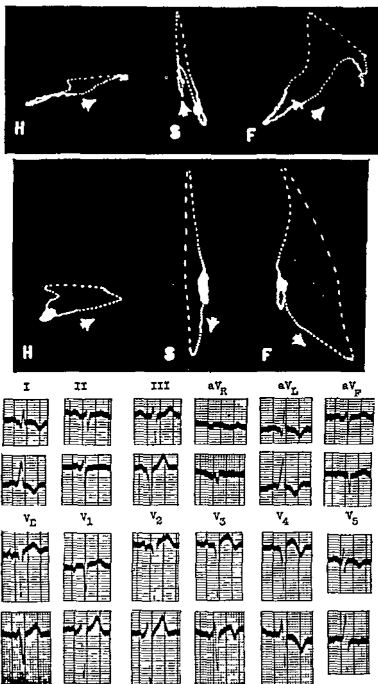


FIGURE 18 Fifty five year old man with anterior myocardial infarction The infarct is concealed in the anomalous tracing (b) but is clearly evident when conduction is normal (a) Inferior infarct is simulated in the anomalous curve (b) The initial and terminal forces are given in TABLE 2 (case 1 from Wolff and Richman[1])



FIGURE 19 Fifty eight year old man with a normal heart The initial and terminal forces are given in TABLE 2 The scalar leads indicate type B

In general there are two main types of WPW syndrome type A which gives positivity in V1 and V2 along with positivity in V5 and V6 and type B which while also giving positive complexes in V5 and V6 displays negative complexes in the right precordial leads I have reviewed all of Rosenbaum s cases and there again all left precordial leads show positivity

In addition the nature and timing of the slurring are most distinctive The early initial slurring (delta wave) either upward or downward ends in a very definite apex In no manner does it simulate the late slurring seen on the crest of the QRS complex during complete bundle branch block If analogies are to be drawn the complexes are at times reminiscent of and often difficult to distinguish from incomplete left bundle branch block

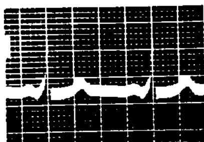
In FIGURE 21 it may be noted in each of the two cases of WPW syndrome that V5 V6 and perhaps lead 1 display a morphology quite similar to incomplete left bundle branch block

My associates and I performed several simple experiments to answer the question as to what sort of premature ventricular beats would produce positivity over the lateral surface of the free left ventricular wall The answer to this question would aid in understanding the positivity in V5 and V6 for these leads record the potential variations over the lateral surface of the free left ventricular wall The importance of this to our study will become apparent a little later

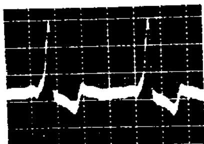
In our experiments from the great multiplicity of the extrasystoles elicited from numerous points of the entire ventricular epicardium (left and right) the following general pattern was distinguished Extrasystoles induced over the left ventricle gave preponderant negativity while the only foci that gave definite positivity over the left apical surface were those provoked in the right ventricle From this we deduced that whatever the nature of WPW syndrome activation must begin somewhere in the right ventricle I believe this result is in accord with Wolff s findings wherein he showed that the initial activation vector pointed to the left and must thus have commenced on the right Narrowing the problem further we now ask what sort of extrasystole this must be to give us the remainder of the pattern of the WPW syndrome It was found that only extrasystoles elicited in the upper right septal mass (or the projection of it on the anterior epicardial surface) will give us positivity both

FIGURE 20 Seve[illegible]ight year old man with extensive myocardial infarction and right bundle-branch block The lesion is concealed in the anomalous tracing (b) but is seen in the tracing with right bundle branch block (a) The initial and terminal forces are given in TABLE 2 (case 2 from Wolff and Richman[10])

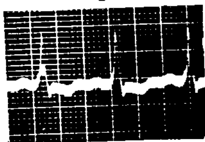
A



B



C



D

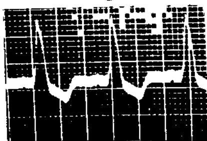


FIGURE 21

over the right epicardium (mainly trabecular zone) and over the apical surface of the left ventricle On the other hand stimulation applied to the lower right septal mass (or its anterior epicardial projection) gives negativity over the trabecular zone but again gives the required positivity at V5 and V6 It is now apparent that we have produced complexes even to the detail of a delta wave that bear a remarkable likeness to those found in clinical examples of the WPW syndrome Please note that I have used the word likeness and have refrained from the use of identical

During any discussion of the WPW syndrome we must keep constantly in mind the normal PS interval to which Rosenbaum called our attention some years ago This implies that while parts of the heart are activated early none can be activated late

At present we are studying septal activation during the production of the special variety of extrasystoles to which I have just alluded Bipolar leads were placed both on the right and left septal surface in order to study the arrival of the activation wave during the normal and the extrasystolic beat As would be expected the right septal surface was in advance of the control during the extrasystolic complex but interestingly enough the left septum showed no delay Moreover since the entire left septum was explored and the sequence of activation during the extrasystoles faithfully mirrored that sequence

FIGURE 22 The quantities 40 5 and 37 5 are expressed in hundredths of seconds

encountered during normal conditions it would be safe to conclude that activa tion was accomplished via the left bundle branch This probably explains Prinzmetal s discovery that when he cut the bundle of His he was unable to produce morphologies similar to the WPW syndrome Actually by doing this he removed the necessary concomitant of an integral normally function ing left bundle

In FIGURE 22 control tracings and complexes of the WPW type are simul taneously recorded with a bipolar lead at point *A* It can be seen that both in the control and in the WPW type complex the interval between the intrinsic deflections at *A* remains the same (0 405 sec) To reiterate since the activa tion process at *A* is the same very likely the activation at *A* occurs through a normally functioning left branch If however the extrasystolic stimulus is delivered too much in advance the P wave becomes incorporated in a non WPW type complex Also it will be noted that the activation process at point *A* is earlier than normal and that the PS interval becomes shorter than normal To obtain an adequate replica of a WPW type complex the PS must remain normal (0 4 sec) and the left sided points such as *A* must be activated in their normal temporal sequence

As I said previously I do not wish to imply that these sudies are on the WPW syndrome rather they are concerned with a similar morphology We have studied if you will these artificial morphologies not the WPW syndrome

If during the course of these experiments we should stop driving both the auricle and ventricle the WPW morphologies would continue to be produced

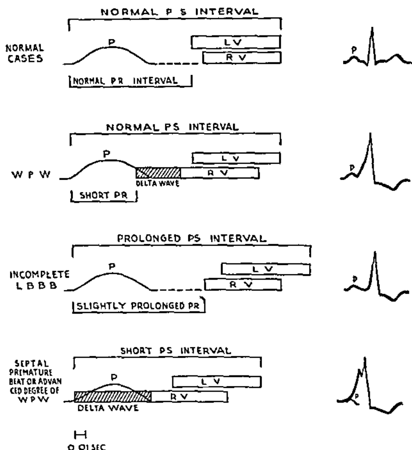


FIGURE 23

for at least several beats It would seem then that such complexes are not necessarily inherent in the technique but could possibly arise *de novo*

FIGURE 23 more or less summarizes the previous discussion

(1) In the normal case both the PR and PS interval are within normal limits

(2) In the WPW syndrome the PS remains normal at the expense of a shortened PR interval The delta wave representing initial premature right septal activation is finally followed by the left ventricular response in a normal sequence

(3) In the left bundle branch block the right ventricle is activated at its usual time while the left ventricle is activated late The morphology of bundle branch block does not change even though the PR interval is prolonged

Normal and Disordered Function of the AV Node Including Accelerated Conduction*

M Prinzmetal and R Kennamer (*Institute for Medical Research Cedars of Lebanon Hospital* and *University of California at Los Angeles Los Angeles Calif*) In recent years experimental studies of the function of the AV node have provided new concepts of the normal and pathological physiology of this very important structure At the same time this new knowledge has made possible a simpler and more logical explanation than was previously available for a number of clinical phenomena It is our purpose to present a brief summary of the salient features of these investigations and to point out their clinical application

From the physiological viewpoint one of the two most important conclusions derived from these studies is the fact that the delay that normally occurs between the end of auricular activation and the onset of ventricular *activation takes place in the AV node and not in the terminal branches of the* conduction system It is obvious that unless there is a delay between the end of auricular activation and the onset of ventricular activation the auricles and the ventricles will contract almost simultaneously This will result in complete loss of auricular function because the auricles cannot empty themselves There is no doubt that this delay occurs at some point between the site of entrance of the impulse into the AV node and the ventricular myocardium This must be true since the time required for the excitation wave to traverse the auricle accounts for only a small fraction of the total time that elapses between the moment of the origin of the impulse at the SA node and the moment of the onset of ventricular depolarization [3] The difficulty in determining the site of the delay more closely has arisen because there is no way of detecting the impulse as it passes down the conduction system in the intact animal Consequently two theories attempting to localize the site of delay have been propounded The first of these originating with Sir Thomas Lewis [24] postulates that the impulse is retarded in passing through the AV node and then progresses rapidly down the bundle of His the bundle branches and the Purkinje system to the ventricular musculature where it causes immediate depolarization The other hypothesis known as the latency theory maintains that the delay does not result from retardation of the impulse at the node but at the terminal endings of the Purkinje system [25] After this delay *has been overcome ventricular depolarization takes place* *No convincing evidence has been offered in support of either theory*

A recent investigation in our laboratory designed to determine the site of the normal delay in auriculoventricular conduction seems to have provided an answer to this question [6] This was accomplished by stimulating with interrupted electrical current first the bundle of His and then the AV node If the ventricular response so produced was delayed at the terminal endings

The work described here has been aided by a grant from the L D Beaumont Trust Fund Cleveland Ohio and by Grant No H 1267 C3 of the National Heart Institute National Institutes of Health Public Health Service Department of Health Education and Welfare Bethesda Md

of the Purkinje system there should have been no appreciable difference in the time interval between the moment of stimulation and the onset of ventricular depolarization whether the stimulus had been applied to the bundle or to the node If the delay occurred in the node the ventricular response resulting from nodal stimulation would have been delayed longer than the ventricular response from stimulation of the bundle Measurements of the intervals between the instant of stimulation and the onset of the R wave of the electrocardiograms that resulted from the stimulation of these two structures showed that these intervals were significantly longer when the impulse was forced to pass through the node than when it originated in the bundle *This direct experiment demonstrates therefore that the delay in normal AV conduction occurs at the AV node and not at the periphery of the conduction system* Hence, the AV node has the important function of delaying auricular impulses

The other important conclusion derived from these studies is the fact that the AV node appears to be composed of cells that seem to transmit impulses through the ventricular conduction system to specific regions of the myocardium Thus in a given animal given cells of the node seem always to control the activation of the same localized portion of the ventricular myocardium Hence the AV node and conduction system may be thought of as analogous to a motor area of the brain and the long tracts descending to the end organ

In these and subsequent experiments the AV nodal region was located by palpation using as a landmark the firm ridge formed by that portion of the auriculoventricular junction lying between the tricuspid orifice and the coronary sinus Exact localization of the node was accomplished by pressing upon portions of this region while observing a continuous tracing When complete AV block was noted it was obvious that the node had been exactly located This was confirmed when the block disappeared upon release of the pressure

The concept that the AV node and the ventricular conduction system constitute functionally at least a sort of central nervous system controlling ventricular depolarization arose from the following observations it was shown that when a constant subthreshold stimulus was applied to the AV node ventricular aberration of a constant type occurred When other parts of the node were similarly stimulated entirely different types of ventricular complexes resulted This suggested that the node is a sort of central nervous system and that from a physiological viewpoint certain parts of the node supply specific parts of the ventricle Further evidence supporting this idea was obtained by Smith and his co workers[27] who showed that strategically placed cuts in the endocardium could produce segmental block with no change in the rest of the ventricles Other experimentally obtained evidence has also suggested that afferent impulses may sometimes pass from the ventricular myocardium to the AV node[5]

Subsequent to these studies a full scale investigation of the WPW syndrome was undertaken This peculiar clinical syndrome consisting typically of a short PR interval and a widened slurred QRS complex is often associated with auricular extrasystoles tachycardia flutter or fibrillation

A large number of theories have been advanced in explanation of the WPW syndrome Of these the most widely accepted states that the auricular impulse passes to the ventricle over congenital anomalous auriculoventricular connections thus short circuiting the normal conduction system Such a short circuit could account for the short PR interval and by prematurely activating a small portion of one ventricle could also explain the wide slurred R wave This theory attempts to explain the occurrence of auricular tachycardia by assuming retrograde ventriculoauricular conduction over the aberrant connections

For various reasons however this explanation of the WPW syndrome although generally accepted has never been completely satisfactory The most painstaking efforts by competent investigators including a most eminent British researcher often failed to reveal any anomalous AV connections in the hearts of classical WPW cases after many months or even years of search Furthermore it has been apparent that this theory could not account in a completely satisfactory manner for the occurrence in the WPW syndrome of auricular flutter or fibrillation by the mechanism of retrograde ventriculoauricular conduction via aberrant bundles since impossibly rapid ventricular rates would be required Still further doubt of the existence of functioning anomalous AV connections has been raised by the observation of Erlanger[8] and subsequent writers[29] that complete heart block invariably results from an interruption of the normal conduction system In our laboratory the bundle of His has been severed in more than a hundred dogs and complete heart block has invariably resulted It would seem that cutting the bundle of His should facilitate conduction by way of accessory AV connections if such connections were actually present yet this phenomenon has never been observed Finally Kent s fundamental observation of the presence of anomalous functionally active anatomic AV bundles[30,3] has never been unequivocally confirmed Recently a careful effort to reproduce Kent s experiments has yielded negative results[33]

In addition to these objections to the theory of anomalous AV connections it has been noted that WPW complexes occur during cardiac catheterization during intrathoracic operations on the lung and in dogs after experimental ligation of a coronary artery[5] The production of WPW aberration by these several dissimilar procedures could hardly have depended upon the function of anomalous AV pathways Furthermore the theory of congenital origin is difficult to reconcile with the increasing numbers of acquired cases coming under observation

When an experimental investigation of the WPW syndrome in dogs was undertaken it soon became apparent that the aberrant complexes could be reproduced regularly by many different methods including mechanical chemical and electrical stimulation of various parts of either ventricle If anomalous AV connections were responsible for the WPW aberration under these circumstances it would be necessary to assume that they were present in practically every dog and that they had intraventricular ramifications as extensive as those of the normal conduction system

Even more significantly it was found that application of a constant electrical

current of subthreshold intensity to the AV node also produced WPW complexes This current evidently interfered with nodal function but still permitted the auricles to drive the ventricles All the variants of QRS complexes observed in the clinical WPW syndrome including the types described by Rosenbaum Hecht Wilson and Johnston[4] were reproduced by disturbing the AV node at different points Disturbance at a given point in the node appeared always to result in the same type of QRS complex Disturbing different points of the node always produced different types of QRS complexes These findings are in conformity with the concept that given nodal cells control specific areas of the ventricle

There now remained the problem of explaining the occurrence of auricular arrhythmias in the WPW syndrome Since it appeared that a nodal disturbance was capable of producing WPW complexes it was suspected that a nodal disorder might also be responsible for the arrhythmias The AV node was therefore made the pacemaker by stimulating it with an interrupted current of greater than threshold intensity By progressively increasing the stimulation rate it was possible to produce in this order supraventricular extrasystoles tachycardia flutter and fibrillation It is pertinent that all these *arrhythmias were part of the clinical WPW syndrome when their exact origin* in man was identified they were usually found to be nodal[4] A comparison of the experimentally produced arrhythmias with those occurring in patients with the clinical WPW syndrome showed that they were identical

Thus experimentally produced disturbances in the AV node resulted in the complete WPW syndrome including all of its typical and atypical forms and variations and all the arrhythmias associated with it

It was clear that the path of the impulse in WPW complexes produced by disturbing the AV node must have been through the normal conduction system and not through aberrant anatomic AV connections such as the Kent bundle The pathways utilized by the impulse during the production of WPW complexes by the numerous other means described above were not as easily determined In order to avoid direct stimulation of any existing anomalous AV connections care had been taken to apply the stimuli in these experiments at points remote from the AV groove Nevertheless further experiments were needed to make a definite determination of the pathway

Ideally the theory of anomalous AV connections could have been examined by cutting all the areas of the heart where such connections could conceivably have been present and then trying to produce the WPW complexes However such a procedure is not feasible The converse experiment was therefore undertaken namely that of cutting the normal conduction system and then attempting to produce WPW complexes by all the methods that had successfully produced them previously with an intact bundle of His When this was done complete heart block occurred as expected *It was impossible to produce any WPW complexes by any of the previously successful methods This experiment clearly indicated that these complexes utilize the normal conduction system and do not require the presence of anomalous anatomical AV connections*

Clinically there is suggestive evidence that complete heart block and the WPW complex are mutually exclusive Two cases in point have been reported

The first case reported by Coelho[34] concerns a 62 year old woman with hyper tension The electrocardiogram taken after posterior myocardial infarction revealed 2 1 heart block associated with short PR intervals and abnormal QRS complexes Subsequently complete heart block developed after which the accelerated conduction or WPW complexes were no longer recorded In the second case reported by Fox and his associates[35] the WPW syndrome was diagnosed in a 70 year old woman After the intravenous administration of 300 mg of Pronestyl 2 1 AV block developed associated with WPW complexes of the conducted impulses After an additional intravenous dose of 200 mg of Pronestyl what appeared to be complete heart block occurred and the WPW beats seemed to disappear Unfortunately the ECG strips were short and exact interpretation was not possible Additional clinical observations of this kind would be desirable

Kinetics of WPW Aberration

By means of a new technique utilizing high speed cinematography of the motions of the ventricles and simultaneous electrocardiograms * the details of the ventricular movements in WPW aberration were studied and correlated with their corresponding electrocardiographic events[5] Camera speeds of as much as 5000 frames per second permitted extremely close correlations between ventricular movements and their corresponding electrocardiographic events This method yielded the information that the kinetics of a usual WPW beat may consist of the following four phases (1) premature contraction of a limited area of one ventricle (2) contraction of the remainder of the ventricles (through the normal mechanism) (3) diastolic relaxation and protrusion of the prematurely contracted area while the remaining parts of the ventricle are still contracted and (4) relaxation of the rest of the ventricles The premature contraction is weak and does not expel blood from the ventricle The diastolic protrusion of this area is often very striking and clearly delineates its location and extent

A detailed correlation of these kinetic events with the simultaneously occurring electrocardiographic phenomena demonstrates that the early slurred R wave or delta wave is associated with the premature localized contraction and that the rest of the R wave may be correlated with the normal contraction of the remainder of the ventricular musculature The ST and T components of the complex are the result of the combined repolarization effects following the two contractions The ventricular component of the WPW complex as a whole is thus seen to be a fusion complex composed of a premature localized contraction in one ventricle and the normal contraction of the rest of the ventricular musculature This conclusion that the WPW beat is a fusion complex is also reached by postulating the presence of anomalous AV connections In this case however there is fusion of the premature impulse with that of the normal conduction system over the accessory connection

* Much of the technical equipment used in this phase of our investigation was designed by L Fields

Accelerated Conduction

Evidence has been obtained suggesting that in WPW complexes (1) the auricular impulse passes to the ventricles over the normal conduction system and not by way of anomalous AV connections (2) the AV node and the intraventricular conduction system seem to be constituted so that given portions of the node always 'supply' the same portion of the ventricular myocardium and no others and (3) the delay in the passage of the impulse from the auricle to the ventricles that normally takes place in the AV node is partially overcome in part of the node This results in premature contraction of part of one ventricle accounting for the short PR interval and the slurred initial portion of the R wave The remainder of the impulse is normally delayed by the rest of the node and activates the remainder of the ventricular myocardium at the normal time This accounts for the portion of the R wave following the delta wave

These findings have given rise to the theory that the WPW complex must result from a disturbance in part of the node that permits that part of the impulse coming to it to pass through it more rapidly than normally This phenomenon has been called accelerated (nodal) conduction

The concept of accelerated conduction appears to explain the mechanism of the WPW syndrome more satisfactorily than any theory previously offered including the theory of anomalous anatomical bundles The experimental procedures that resulted in accelerated conduction have reproduced the clinical features of the WPW syndrome completely and faithfully The aberrant complexes produced in the dog are identical with those seen in patients including the short PR interval the delta wave the wide aberrant R wave and even the ST and T wave changes All variants of the syndrome observed clinically were produced experimentally and all the arrhythmias reported in clinical cases were produced in the dogs used in the experiments

The clinical WPW syndrome that is usually thought to be congenital is not however the only condition that depends upon accelerated conduction It has become increasingly evident that WPW aberration can be acquired Indeed our experience has indicated that this type of aberration is more commonly acquired than congenital In the last few years we have observed at least twenty patients in whom the aberration was obviously acquired either as a result of disease or as a functional disorder the aberration in these cases arose under a variety of conditions and was known not to have been present previously The possibility of acquiring this condition is strongly indicated by the fact that the aberration was produced consistently in practically every dog used in the experiments It is unreasonable to assume that each experimental animal and each of the patients with acquired WPW was equipped with congenital accessory anomalous AV connections

In acquired cases the WPW aberration may be transient or intermittent A considerable incidence may therefore be missed unless tracings happen to be made while the aberration is present Reference has already been made to the occurrence of WPW aberration during intrathoracic operations and

during cardiac catheterization although the majority of cases in our experience in this country in which acquired WPW aberration has been observed have been instances of myocardial infarction In South America however de Mesquita[36] has observed acquired cases apparently attributable to Chagas disease Usually the lesion has involved the posterior wall and presumably the AV nodal region In view of the temporary or intermittent presence of the aberration in some of these patients the nodal disturbance in such instances is presumed to have been due to reversible processes such as ischemia edema or reflex changes

In other patients the acquired nodal disturbance has been proved by post mortem examination to have been due to definite extensive organic pathological changes in the node Five such examples have come to our attention In three of the cases of acquired WPW aberration developed after the onset of posterior wall myocardial infarction Careful miscroscopic examination of the nodal region in two cases by Goldblatt[37] and Lev[38] disclosed marked involvement of this area by fibrotic scar tissue representing part of the healed posterior wall infarct *In the third case the fibrotic area was considered to be in the* upper limits of normal

For the other two cases which were examples of Chagas disease we are indebted to de Mesquita[36] Both of these patients presumably developed WPW aberration during acute illnesses The hearts were examined by Lev[38] Histological sections of the nodal area in one case showed a marked inflammatory process in this region characterized chiefly by round cell infiltration and edema In the other case the node was normal but the tissue immediately adjacent to it was severely inflamed In these two instances of Chagas disease the auriculoventricular junctional regions are now being carefully studied by Lev in an effort to determine whether anomalous anatomical connections can be demonstrated A complete report will be made after the completion of the studies In the other three cases such investigations were not carried out

Miscellaneous Types of Ventricular Aberration Associated with AV Nodal Disorders

It is obvious that accelerated conduction is not the only disturbance of the AV node that can give rise to ventricular aberration It is well known for example that aberrant ventricular complexes of nonspecific configuration may occur in association with abnormal nodal rhythms such as tachycardia In the presence of complete heart block due to AV nodal disease the bizarre aberrant complexes of so-called idioventricular rhythm appear as well as other varieties of aberrant ventricular complexes that will be discussed later[39]

In a series of experiments using dogs the AV node was irritated and traumatized mechanically chemically and electrically These procedures resulted in a variety of ventricular aberrations including complexes identical to those seen in complete and incomplete right and left bundle branch block ventricular extrasystoles ventricular tachycardia bidirectional ventricular tachycardia and idioventricular rhythm In association with many of these aberrations

various degrees of AV block were present indicating the presence of a nodal disorder

All of these ventricular aberrations produced by AV nodal disturbances have clinical analogues—cases in which there exist various degrees of heart block nodal rhythms or other evidence of nodal disorder and at the same time one or more of the numerous ventricular aberrations described above * It would seem therefore that a certain number of clinical cases in which both nodal disturbances and aberrant ventricular complexes are present can be explained best by the concept that the nodal disorder is responsible for the ventricular aberration Otherwise it is necessary to postulate more complex mechanisms requiring the presence of multiple disturbances involving the node and one or both ventricles sometimes alternating rapidly between the two ventricles

Thus it can be seen that interference with the function of so tiny a structure as the AV node can give rise to a wide variety of abnormalities These may be briefly summarized as follows (1) heart block of various types and degrees (2) accelerated conduction (congenital or acquired) through part of the node (short PR aberrant QRS) or through the entire node (short PR normal QRS) and (3) other nodal disorders (manifested in many cases by partial or complete AV block)

The same interference can give rise to ventricular aberrations identical to (1) ventricular extrasystoles left right and indeterminate (2) complete and partial left and right bundle branch block complexes, (3) ventricular tachycardia (4) bidirectional ventricular tachycardia (5) idioventricular beats (6) nonspecific types of aberrant ventricular complexes and (7) retrograde but normal upright P waves following normal or abnormal QRS complexes † The nature of this latter peculiar disorder is not understood no heart block is present because there are as many P waves as QRS complexes

All of these disorders have been produced experimentally and have also been seen clinically By conceiving of them as primarily nodal disturbances due to abnormalities of the delaying function of the node rather than as simultaneously present nodal and ventricular disorders their mechanism becomes readily understandable Accelerated conduction indicates partial loss of the delaying function of all or part of the node, while AV block represents too much delay in all or part of the node Since the cells and fibers of the node and the intraventricular conduction system are functionally separated from one another physiological disorders of parts of the node will result in physiological disorders in corresponding parts of the ventricles These disorders manifest themselves electrocardiographically as aberrant ventricular complexes of many kinds with or without changes in the PR interval

This experimentally derived anatomically supported and relatively simple concept would seem to provide a clearer explanation than hitherto available for many ventricular aberrations encountered clinically

* For some of these cases we are indebted to Roy W Scott and Herman Hellerstein of Cleveland Ohio

† A Ravin of Denver Colo has kindly called to our attention an example of the normal P wave gradually moving into and behind the abnormal QRS complex in a case of WPW It would appear impossible for such a phenomenon to occur in accordance with an abnormal anatomical bundle

A final opinion concerning the validity of the theory we have summarized briefly however will depend upon further research Much more histological study especially of the type now being carried out by Maurice Lev is required The work entails months or years of painstaking effort a large number of cases must be examined in order to provide valid evidence for or against this concept It may develop for example that some cases of WPW syndrome are indeed dependent upon congenital anomalous anatomical AV connections while others may result from an AV nodal disorder In any event a patient and open minded attitude should be maintained until conclusive proof is available

Discussion

F F Rosenbaum The phenomenon of anomalous atrioventricular excitation finds considerable application in the sort of problems discussed in this panel Just as the study of bundle branch block added much to our understanding of the genesis of the electrocardiogram in the WPW syndrome we have another opportunity to break the QRS complex down into component parts Seemingly in this anomaly we have one element of the ventricle activated much earlier than the remaining normally activated element The time relationship of the activation waves of the two ventricular elements to each other is not unlike that seen in bundle branch block yet we rarely see ventricular complexes that really resemble those of either right or left bundle branch block It seems therefore that the spread of the impulse through the ventricle that is activated early is in some fashion unlike the normal activation wave and does not travel through either the right or left main branch of the His bundle or through their ramifications

One question that has occurred to me concerns the belief that anomalous atrioventricular excitation is due to a more rapid spread of the impulse through damaged atrioventricular nodal tissue Why under these circumstances should diseased specialized conduction tissue elements transmit an impulse more rapidly than normal when the reverse is true when this zone of the myocardium is altered by such diseases as rheumatic myocarditis or acute myocardial infarction?

In reference to the experimental and clinical observations referred to by Sodi Pallares I should like to say that I feel we must avoid placing too much weight upon superficial resemblances of electrocardiographic tracings If we believe that a recorded observation actually represents anomalous atrioventricular excitation we must insist that there be a delta wave and a sharp terminal deflection in the ventricular complex just as we insist upon these criteria in making the diagnosis in the random instances that come to us in our clinical experience

There appear to be rare instances of the WPW syndrome in which the supraventricular impulse spreads to the ventricles only through the anomalous mechanism It is difficult to believe that in these patients life is dependent solely upon an electrotonic or mechanical stimulation of the ventricles by the auricles Some structural muscular bypass seems far more likely to insure the continued regular ventricular activity demonstrated by these patients Instances of this disorder in more than a single member of the same family and

its occurrence in association with other cardiac anomalies are additional reasons for believing that some structural anomalous bypass is present

It seems not improbable that there are several mechanisms of pre-excitation but it is my feeling that in most of the instances we encounter in our routine *clinical observations we are dealing with a situation in which there is a structural bypass* in or near the interventricular septum possibly arising from the lower portion of the atrioventricular node and having broad ramifications in the subepicardial myocardium of the posterior ventricular wall usually on the right and occasionally on the left side of the septum

P Rijlant (*University of Brussels Brussels Belgium*) I did not want to interfere with the discussion of the WPW syndrome but I can confirm some of the physiological facts upon which Prinzmetal has based his theory The delay in the auricular ventricular conduction is due not so much to the His bundle but to slow conduction within the AV node Pharmacological action is also limited to the AV node Twenty five years ago measurements of conduction velocity were already quite accurate and it was then possible to show that by application of acetylcholine on the AV node the normal delay could be increased by at least 50 to 100 per cent while an equal amount of acetylcholine applied to the His bundle did not change conduction The action of the vagus on the conduction system is also confined to the AV node and not to the His bundle or its branches

H H Hecht It seems to me that Prinzmetal s theory and his experiments require some comments concerning the possibility of accelerated conduction in damaged tissue

C Brooks (*State University of New York College of Medicine Brooklyn N Y*) An answer can be given but I am not certain that it is correct It is true that the excitability and speed of conduction in tissues depend in large measure upon factors maintaining membrane polarization The passage of cathodal current through a tissue creates a state of instability or hyperexcitability (catelectrotonus) An injury or an anoxic area that creates localized depolarization will serve to generate a current of injury A cathodal current flow thus occurs through adjacent tissues that should theoretically render them more excitable A localized lack of oxygen or some other essential material should also reduce the effectiveness of reactions maintaining membrane polarization Therefore in these areas near an injury or in areas suffering some marginal deficiency weaker stimuli should be effective a quicker breakdown of the membrane should occur and conduction should be faster It seems to me that under abnormal conditions faster than normal conduction in a heart is possible

J S Robb (*State University of New York College of Medicine Syracuse N Y*) I should like to point out again that there are very great individual differences in the structure of the conduction system There is an AV node there is a bundle and there are branches but the particular number of branches and the particular distribution varies from individual animal to individual animal There can be anomalous branches

I desire to stress another point Concerning leukocytic infiltration or replacement of normal tissue by fibrosis it seems to me that there is a possibility

that has not been discussed It is not necessarily damaged tissue that is conducting early It may be that in this mass of pathology we have a strand or two of normal conducting tissue going down and that these strands are conducting faster than the rest of the tissue because the remaining tissue while not sufficiently different to make its conduction time abnormally long could still delay conduction enough to produce a variation in rates of conduction Prinzmetal s experiments might be interpreted on this basis

A Pick (*Heart Station Michael Reese Hospital Chicago Ill*) I do not think that anyone doubts that pre excitation beats are fusion beats but the real question is how are they produced? Under normal conditions the impulse reaches both bundle branches and activates both ventricles almost simultaneously In beats of pre excitation contour one portion of the ventricles is excited prematurely This may be due either to the rise of another simultaneous impulse at the point of earlier activation or to the use of two pathways by the single sinus impulse one of which bypasses the obstacle of the AV node and causes some portions of the ventricles to be activated ahead of others Both of these mechanisms of course will produce fusion beats of similar contour It is our task to decide which of the two is acting in the true pre excitation syndrome To do this we must examine the evidence in each individual case and we also must have a precise definition of true pre excitation According to the present state of knowledge one should I believe restrict the term pre excitation only to beats having a delta wave and a foreshortened PR interval which remains fixed in a series of such beats This was not the case in some examples described by the panelists in which anomalous ventricular complexes had been produced by mechanical stimulation of the ventricular septum In these cases I believe we are dealing with an AV dissociation caused by stimulation of a ventricular focus operating at a rate close to that of the sinus node That this is possible has been demonstrated experimentally by Scherf[8] Contrariwise in my opinion in real pre-excitation an anomalous bypass of the AV node must be present since otherwise we could neither explain the occurrence of predominantly supraventricular tachycardia in the syndrome nor the persistence of pre excitation complexes during auricular fibrillation Further strong evidence for this view is (1) the anatomical demonstration of such a bypass in over half of the examined cases (2) the experimental reproduction of the entire syndrome by Butterworth and Poindexter[40] (3) the fact that pre excitation may be found in association with AV block and finally (4) the fact that on occasion ectopic impulses can be shown to arise with the anomalous AV bridge

Summary and Conclusion

H H Hecht It seems to me that it should be possible to derive a satisfactory synthesis of the somewhat divergent thoughts that have been expressed in this panel It is clear that the ventricular muscle has the capacity to respond to two action currents (double excitation) followed by one effective mechanical beat Butterworth and Poindexter s experimentally produced fusion complexes[40] which they introduced as an explanation for anomalous atrioventricular excitation are typical of the many experiments (beginning

with Lewis's demonstration[41]) that attest to this fact. When this takes place some segments of ventricular muscle respond to the impulse that arrives first, the remainder of the muscle responds to a slightly later second wave of excitation. Such an event results in a ventricular "fusion beat," a term that implies no more than that the electrocardiographic complex is the resultant of two almost simultaneous stimuli. Observation of the mechanical function of the heart in instances of this kind seems to support the idea of double excitation by demonstrating a slight mechanical asynchrony with the pre-excited part responding slightly before the remainder in some, although not in all, of the reported cases.

We may now single out at least three of the more likely causes for such a fusion phenomenon.

(1) An area of ventricular muscle may spontaneously depolarize very late in the diastolic period or may be made to do so by external stimulation. Part of the ventricular musculature will be depolarized from and will respond to this ectopic focus. Propagation, however, is only partially successful because normal atrioventricular conduction has resulted in the excitation of the remainder of the ventricular myocardium. Such fusion extrasystoles of ventricular origin do not, of course, show a post extrasystolic pause. The configuration of QRS under those circumstances may not depend only on fusion and pre excitation but also on the location of the area responding to the abnormal focus.[9, 18] This seems to be substantiated by the observations of Sodi Pallares and his associates.[19] Experiments previously mentioned[9] and the examples observed following catheterization injury[72] may perhaps belong to this type.

(2) Ectopic foci of this kind (fusion extrasystoles) have no bearing on the mechanism of anomalous atrioventricular excitation except to demonstrate the fact that double excitation is possible. In anomalous atrioventricular excitation fusion beats may occur over long time periods and are essentially independent of sinus irregularities and various degrees of partial AV block. They disappear when the impulse is displaced into the lower nodal region, the common stem of the His bundle, or when complete AV block is induced. This type of double excitation may be considered a distinct clinical entity, the WPW syndrome. This syndrome may or may not be associated with organic heart disease (often masking or modifying an otherwise abnormal electrocardiogram) and it is frequently accompanied by a tendency to paroxysmal supraventricular tachycardia. During these paroxysms either entirely normal, entirely abnormal, or intermediate forms of QRS complexes may be recorded. The attacks may be long lasting or they may be of very short duration. In the latter case they may escape attention entirely or may be casually discovered, for instance, during the manipulation of a cardiac catheter.

Evidence for the congenital nature of the WPW syndrome is still mostly circumstantial but strong. The syndrome has been reported with various types of congenital cardiac malformations.[5, 7, 14, 42-45] By itself this relationship proves little since its true incidence in the parent population is not known. Reports of hospital series are obviously unreliable because patients with the disorder are not likely to seek medical advice. If Graybiel's series of electro

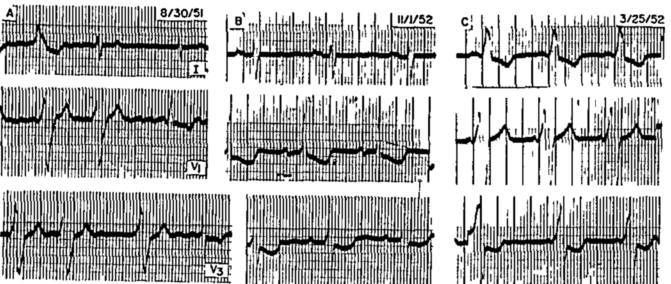


FIGURE 24. Masked anomalous atrioventricular excitation in a 29 year old veteran (L. T.) with rheumatic mitral stenosis. Atrial fibrillation with normal and abnormal conduction is present in A. Normal conduction was observed in several subsequent tracings (B) that were typical of right ventricular and left atrial enlargement. Normal conduction was present throughout the continuously monitored operative course. Anomalous conduction appeared again 6 weeks after surgery (C). The pre excitation wave occupies a larger portion of the QRS than is usual for the syndrome, but the short PR segment and the characteristic configuration of QRS in V_1 and V_3 establish the diagnosis. In retrospect, the abnormal complexes in A are the result of anomalous excitation. This was not an acquired WPW syndrome following mitral valve surgery, as had been assumed at first glance.

cardiograms on normal aviators[46] is an indication the incidence in the adult population would be 0.001 per cent. In 282 consecutive patients with congenital cardiac malformations observed by us during the last 3 years anomalous atrioventricular excitation occurred twice or 70 times as frequently as expected. Other strong evidence for the congenital nature of the syndrome is *the increasing frequency of its recognition in infants and in the newborn*[25, 47] and the occurrence of the full blown syndrome in families as already mentioned by Wolff and Rosenbaum in this panel and by others[7, 48, 49]. Proof of the heredity of the syndrome would lie in the observation of its occurrence in identical twins which I believe has not been reported so far.

We need not discuss the question whether the demonstration of accessory bundles connecting the atria to the ventricles in some autopsied cases constitutes valid proof that anomalous atrioventricular excitation occurs over such pathways. This has been an attractive hypothesis although the famous bundle of Kent whose very existence is in doubt certainly cannot be implicated. Robb has indicated and Segers and his co-workers[50] have published evidence that such paths may exist even within the septum. It is of interest in this connection that embryonic tissue is capable of impulse propagation long before a recognizable conduction system has been established. One may speculate that embryonic rests may bridge the atrioventricular junction supplementing normal conduction pathways.

The electrocardiographic features of pre-excitation with short PR may occur as an *acquired lesion* and I believe instances of this kind should be separated both from ectopic fusion beats and from the clinical syndrome discussed above. This may indeed be the consequence of some specific manipulation involving the atrioventricular junction. The observations mentioned by Prinzmetal and by Sodi Pallares belong to this type of anomalous excitation as would some of the examples mentioned by Scherf and his co-workers[6]. The cases reported by Kossmann[51] in which the syndrome was observed following cardiac catheterization would also belong to this type although it is possible that these may belong to the group of fusion extrasystoles. One should be careful however *to be sure that the acquired syndrome is not simply an* unmasking of a previously well hidden congenital anomaly. FIGURE 24 illustrates the example of a 27 year old veteran with rheumatic heart disease mitral stenosis and predominant right ventricular hypertrophy. During a period of atrial fibrillation abnormal complexes were observed that were absent on many subsequent occasions even during conversion by quinidine and during the surgical procedure (mitral commissurotomy). On a routine follow up examination six months after surgery classical anomalous atrioventricular excitation was revealed to be present with ventricular complexes nearly identical to those observed previously during the episode of fibrillation. This was not then an acquired anomalous atrioventricular excitation but one that had remained uncovered for long periods between the examinations (even during intracardiac surgery). The case could easily have been listed as an example of the acquired type. Similar examples have been reported by Lyle[5].

Prinzmetal's concept of accelerated conduction may be considered a varia

TABLE 3

SUBDIVISIONS OF VENTRICULAR FUSION PHENOMENA (DOUBLE VENTRICULAR EXCITATION)

Type A (usually sporadic)
 (1) Fusion extrasystoles
 Ectopic ventricular focus occurring late in diastole with fortuitous superposition of normal excitation no post extrasystolic pause (septal origin?)
 (2) Ectopic foci from high septal regions
Type B (usually continuous)
 Anomalous atrioventricular excitation inherited and acquired types
 (1) Inherited Wolff Parkinson White syndrome with frequent episodes of paroxysmal atrial tachycardia (congenital accessory conduction pathways?)
 (2) Acquired commonly associated with cardiac disease but not with atrial tachycardia (partially accelerated a v conduction?)

tion of the concept that pre excitation occurs because some strands of conducting tissue wherever they may be located circumvent the normal delay usually encountered in passage through the AV node Prinzmetal applies this concept specifically to the AV nodal region and assumes the presence of differential conduction through this region This is longitudinal dissociation of the AV node which in the past, has been implicated as the cause of certain conduction anomalies such as the occurrence of retrograde P waves in complete (forward) AV block or the forward excitation of the ventricles by retrograde conducted P wave reciprocal beats It may be related to the supernormal phase in conduction that Brooks had in mind Brooks has implied—as have others—that general hyperexcitability may become a characteristic of damaged tissue One may add that perhaps a release of potassium from damaged cells with a lowering of the intracellular potential closer to the firing level may be involved At any rate differential conduction is the basis of certain experiments dating from Schmitt and Erlanger[63] which led to the formulation of the concept of re entry and of circus movement in the mammalian heart I am delighted to see Prinzmetal looking at himself from the other side of the fence!

In conclusion we have discussed an anomaly in ventricular excitation that on the face of it may be of interest only to the clinical interpreter of an electrocardiogram We chose the topic however because its detailed analysis may hold some clues to the spread of excitation over cardiac musculature in general The several divergent views we have discussed do not appear contradictory Perhaps TABLE 3 may be acceptable to all participants as a working hypothesis

References

1 SEGERS M J LEQUIME & H DENOLIN 1944 L activation ventriculaire precoce de certains coeurs hyperexcitables Étude de l onde Δ de l électrocardiogramme Cardiologia 8 113
2 WOLFF L J PARKINSON & P D WHITE 1930 Bundle branch block with short PR interval in healthy young people prone to paroxysmal tachycardia Am Heart J 5 685
3 WILSON F N 1915 A case in which the vagus influenced the form of the ventricular complex of the electrocardiogram A M A Arch Internal Med 16 1008
4 ROSENBAUM F F H H HECHT F N WILSON & F D JOHNSTON 1945 The potential variations of the thorax and the esophagus in anomalous atrioventricular excitation (Wolff Parkinson White Syndrome) Am Heart J 29 281

5 PRINZMETAL M P KENNAMER I CORDAY J A OSBORNE J FIELDS & L A SMITH 1952 Accelerated Conduction Grune & Stratton New York N Y
6 SCHERF D S BLUMENFELD & I MUELLER 1952 A V conduction disturbance in the presence of the pre excitation syndrome Am Heart J 43 829
7 ÖHNELL R F 1944 Pre-excitation a cardiac abnormality Acta Med Scand Suppl 152
8 KOSSMANN C E & H H GOLDBERG 1947 Sequence of ventricular stimulation and contraction in a case of anomalous atrio-ventricular excitation Am Heart J 33 308
9 WOLFF L & P D WHITE 1948 Syndrome of short P R interval with abnormal QRS complexes and paroxysmal tachycardia A M A Arch Internal Med 82 446
10 WOLFF L & J L RICHMAN 1953 The diagnosis of myocardial infarction in patients with anomalous atrio-ventricular excitation (Wolff Parkinson White Syndrome) Am Heart J 45 545
11 LANGENDORF R M LEV & R PICK 1952 Auricular fibrillation with anomalous A V excitation (WPW Syndrome) imitating ventricular paroxysmal tachycardia A case report with clinical and autopsy findings and critical review of the literature Acta Cardiol 7 241
12 LEVINE H D & J C BURGE JR 1948 Septal infarction with complete heart block and intermittent anomalous atrioventricular excitation (Wolff Parkinson White Syndrome) Histologic demonstration of a right lateral bundle Am Heart J 36 431
13 PICK A & L N KATZ 1955 Disturbance of impulse formation and conduction in the pre excitation (WPW) syndrome—their bearing on its mechanism Am J Med 19 759
14 LEV M S GIBSON & P A MILLER 1955 Ebstein s disease with Wolff Parkinson White Syndrome Report of a case with a histopathologic study of possible conduction pathways Am Heart J 49 724
15 WOOD F C C C WOLFERTH & G D GECKELER 1943 Histologic demonstration of accessory muscle connections between auricle and ventricle in a case of short P R interval and prolonged QRS complex Am Heart J 25 454
16 KIMBALL J L & G BURCH 1947 The prognosis of the Wolff Parkinson White Syndrome Ann Internal Med 27 239
17 HECHT H H & L RITZMANN 1950 The potential variation of the epicardial and endocardial surfaces in anomalous atrioventricular excitation Am J Med 8 527
18 SODI PALLARES D J SOBERON I THOMSEN B L FISHLEDER & A ESTANDIA 1948 Contribucional estudio del sindrome de W P W por las derivaciónes intracavitarias Arch inst cardiol Mex 8 1
19 GRISHMAN A I G KROOP & M F STEINBERG 1950 The course of the excitation wave in patients with electrocardiograms showing short PR intervals and wide QRS complexes (Wolff Parkinson White Syndrome) Am Heart J 40 554
20 HECHT H H & L A WOODBURY 1950 Excitation of human auricular muscle and the significance of the intrinsicoid deflection of the auricular electrocardiogram Circulation 2 37
21 GRISHMAN A & H L JAFFE 1951 Spatial vectorcardiography wide QRS complexes with short PR interval (The Wolff Parkinson White Syndrome) J Mount Sinai Hospital 18 208
22 BERKUN M A I H KESSELMAN F DONOSO & A GRISHMAN 1956 The spatial ventricular gradient Intermittent Wolff Parkinson White Syndrome intermittent left bundle branch block and ventricular premature contractions Circulation 13 562
23 PRINZMETAL M F CORDAY I C BRILL R W OBLATH H E KRUGER J FIELDS W FLEIG A GOLDMAN H KARPMAN S R KENNAMER J A OSBORNE A L SELLERS & L A SMITH 1952 The Auricular Arrhythmias Charles C Thomas Springfield Ill
24 LEWIS T 1925 The Mechanism and Graphic Registration of the Heart Beat 3rd ed Shaw & Sons Ltd London England
25 ERLANGER J 1912 Observations on the physiology of the Purkinje tissue Am J Physiol 30 395
26 OSBORNE J A E CORDAY J FIELDS R KENNAMER L A SMITH & M PRINZMETAL 1951 Studies on the mechanism of ventricular activity I The nature of the P R interval Am Heart J 42 503
27 SMITH L A R KENNAMER & M PRINZMETAL 1954 Studies on the mechanism of ventricular activity IV Ventricular excitation in segmental and diffuse types of experimental bundle branch block Circulation Research 2 221

28 Erlanger J 1943 Correspondence Am Heart J 26 419
29 Borduas J L I Rakita R Kennamer & M Prinzmetal 1955 Clinical and experimental studies of accelerated auriculo ventricular conduction Circulation 11 69
30 Kent A F S 1892-1893 Researches on the structure and function of the mammalian heart J Physiol 14 233
31 Kent A F S 1913 The structure of the cardiac tissue at the auriculoventricular junction J Physiol 47 17
32 Kent A F S 1913 Observations on the auriculo-ventricular junction of the mammalian heart Quart J Exptl Physiol 7 193
33 Frau G G C Maggi & A Agostini 1953 An experimental study of A V conduction over fibers of the bundle of Kent Acta Cardiol 8(3) 225
34 Coelho E 1945 Nova contribuicao para o estudo do sindroma de Wolff Parkinson White (W P W) Amat Iusit 4 603
35 Fox T T J Weaver & H W March 1952 On the mechanism of the arrhythmias in aberrant atrioventricular conduction (Wolff Parkinson White) Am Heart J 43 507
36 Mesquita Q H de 1955 Personal communications
37 Goldblatt H 1955 Personal communications
38 Lev M 1935 Personal communications
39 Rakita L R Kennamer S Rothman & M Prinzmetal 1957 Studies on the mechanism of ventricular activity XV Experimental and clinical observations on ventricular aberration resulting from abnormal A V nodal function A M A Arch Internal Med In press
40 Butterworth J S & C A Poindexter 1944 Fusion beats and their relation to the syndrome of short PR interval associated with a prolonged QRS complex Am Heart J 28 149
41 Lewis T 1911 Observations upon disorders of the heart s action Heart 3 279
42 Bodlander J W 1946 Wolff Parkinson White Syndrome in association with congenital heart disease Am Heart J 31 785
43 Stein M H 1948 Wolff Parkinson White Syndrome in case of congenital heart disease Am Heart J 35 140
44 Kleiber E F 1949 Wolff Parkinson White Syndrome with congenital heart disease Pediatrics 4 210
45 Bartholomew L G & H B Burchell 1952 Wolff Parkinson White Syndrome associated with situs inversus report of case simulating myocardial infarction electrocardiographically Proc Staff Meeting Mayo Clinic 27 98
46 Graybiel A R A McFarland D C Gates & F A Webster 1944 Analysis of the electrocardiogram obtained from 1000 young healthy aviators Am Heart J 27 524
47 Kreidberg M B & T A Dushan 1953 Paroxysmal auricular tachycardia associated with Wolff Parkinson White Syndrome in a newborn infant J Pediat 43 92
48 Willis W H & C C Shepard 1953 The familiar incidence of certain unusual diseases North N Y Med J 10 19
49 Averill J H 1956 Wolff Parkinson White Syndrome occurring in brothers Am Heart J 51 943
50 Seger M T Sanabria J Lequime & H Denolin 1947 Le syndrome de Wolff Parkinson White Mise en évidence d une connexion a v septale directe Acta Cardiol 2 21 1047
51 Kossmann C E A R Berger S A Briller B Radar & J Brumlik 1950 Anomalous atrioventricular excitation produced by catheterization of the normal human heart Circulation 1 902
52 Lyle A M *1953 Latent Wolff Parkinson White Syndrome Am Heart J 46 49*
53 Schmitt F O & J Erlanger 1928 Directional differences in conduction of impulse through heart muscle and their possible relation to extrasystolic and fibrillary contractions Am J Physiol 87 326

Part III Cardiac Recovery

RECOVERY OF CARDIAC MUSCLE A PARTICULAR PROBLEM

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When compared to other tissues the recovery process in cardiac muscle is unique as has been demonstrated in the records of monophasic action potentials described earlier in this monograph Reference was made to a figure from the book by Brooks *et al*[1] to show that even in cardiac tissues the form of the action potential differs For example compared to ventricular muscle a plateau during recovery is lower and longer in Purkinje fibers for comparable rates and is absent in atrial muscle Both Cole and Weidmann in the section of this monograph dealing with cellular events described a few monophasic records of nerve that looked like a foreshortened version of the cardiac action potential

It appears that the answers to many questions relating to the restitution of excitability in any tissue have been and will be found with the least experimental difficulty in cardiac muscle Whether these will be applicable to all excitable tissues is problematical

One of the principal objectives of this section on cardiac recovery is to re emphasize the physiological differences in the time course of repolarization as compared to depolarization ascribable probably in large part to mechanical contraction of the heart soon after the beginning of excitation

As early as 1921 Wilson and Herrmann recognized that the form and direction of the deflection resulting from the decline of excitation were determined by at least two different factors the form of the preceding QRS and such local factors as cooling Although at the time they concluded from experimental stimulation of each ventricle in dogs that the duration of the excited state was approximately uniform in all parts of the ventricular muscle there was one conflicting experiment in which the left ventricle remained intermittently refractory longer than a simultaneously stimulated point on the right ventricle The significance of the finding was minimized at the time but was later found to have considerable importance in the elaboration of the concept of the ventricular gradient first mentioned by Wilson *et al*[2] in 1931 and further elaborated by these investigators[4] in 1934 Although the gradient was also spoken of as the electrical axis of QRST Bayley s[5] recent interesting vector analysis would indicate that the gradient is not an existent electromotive force but rather a directional derivative of the duration of the excited state at any point in the ventricular muscle dependent upon the spatial orientation of that point The gradient as a measure of differences in both the rate and duration of repolarization was touched upon by Hecht and Schaefer earlier in these pages

Although the ventricular gradient should be a valuable clinical measurement the time consuming task of determining it has limited its use Briller s[6]

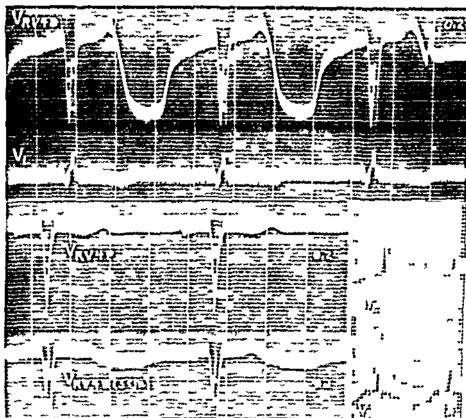


FIGURE 1 Intracardiac lead in a 28 year old Negro male with unknown heart disease *displaying a late large negative potential possibly caused by hyperpolarization* The upper record ($V_{RV(D)}$) from the right ventricle made simultaneously with the potential of the left arm (V_L) shows a spontaneous disappearance of the potential at the end of the strip The lower records were made with a double electrode catheter in the right ventricle with the electrodes 3 cm apart The proximal electrode recorded the probable true potential of the cavity ($V_{RV(P)}$) and the distal electrode recorded the negative afterpotential but in lesser degree than initially ($V_{RV(D)}$) Note the occurrence of this potential near the end of the T wave and its persistence for almost 0 3 sec into the T P interval The time lines represent 0 2 sec In the lower right hand corner are leads aV_F and V_L in a 67 year old woman who had received quinidine for the treatment of atrial fibrillation within the preceding 24 hours Note the late downward deflection fused with the T wave and occupying the entire T P segment The time lines represent 0 04 sec String sensitivity is normal except as indicated

analogue computer which he describes elsewhere in this monograph bodes well for ultimate circumvention of this practical obstacle and his data will reveal that magnitude is perhaps more important than direction in differentiating the abnormal from the normal even though present clinical methods are more concerned with the latter[7] Schaefer has suggested this in relating the magnitude of the gradient to the magnitude of the area of QRS

In the spatial configuration it has seemed to us that possibly not all the desired or available information is incorporated in the ventricular gradient and

for this reason we have made some empirical studies on the relationship of the spatial areas of QRS and T in terms of electrical work done during each process with the initial assumption that the heart generator is a fixed position varying moment dipole[8] Briller elaborates on these studies later in this part of the monograph The concept may have serious limitations in view of Schaefer s statement that less than 10 per cent of the total electricity generated reaches the surface and in view of W Trautwein s demonstration that the gradient is not related to the state of dilatation or to cardiac work

An observation of interest is presented in FIGURE 1 noted during catheterization of the right ventricle in a Negro male subject with unknown heart disease A catheter electrode displayed unusual negative displacement of the T P seg

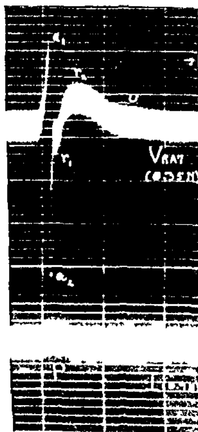


FIGURE 2 Enlarged electrogram (V_{RAT} upper record) made from the interior of the right atrium simultaneously with lead I (lower record) in a patient with complete atrioventricular block The symbols are as follows a_1 a_2 accession deflections r_1 r_2 regression deflections U afterpotential P P wave in lead I The time lines represent 0 2 sec Gain is indicated on the records (From C I Kossmann in *The Medical Clinics of North America* 1950 vol 34 p 833)

ment when the electrode was obviously touching the endocardium This is clear from the fact that the large negative after potential disappears at the end of the record Further when a double electrode catheter was used as shown in the lower strip the deflection was absent from the record made from the proximal electrode but was present in an electrode 3 cm more distal A deflection of this kind has also been seen when recording intracellular potentials In the lower right hand corner of the figure are shown similar deflections in leads aV_F and V_6 in a 67 year old female who had received 1 8 gm of quinidine in the preceding 24 hours

FIGURE 2 shows a right atrial electrogram in a patient with complete A V block displaying an afterpotential labeled U It is shown to demonstrate that an afterpotential occurs in human atrial muscle

References

1 BROOKS C McC B F HOFFMAN E E SUCKLING & O ORIAS 1955 Excitability of the Heart Grune & Stratton New York N Y

2 WILSON F N & G R HERRMANN 1921 An experimental study of incomplete bundle branch block and of the refractory period of the heart of the dog Heart 8 229

3 WILSON F N A G MACLEOD & P S BARKER 1931 The T deflection of the electrocardiogram *Trans Assoc Am Physicians 46 29*

4 WILSON F N A G MACLEOD P S BARKER & F D JOHNSTON 1934 The determination and the significance of the areas of the ventricular deflections of the electrocardiogram Am Heart J 10 46

5 BAYLEY R H 1955 Vector analysis of the T deflection of the electrocardiogram Am Heart J 50 844

6 BRILLER S A N MARCHAND & C E KOSSMANN 1954 An electronic analog computer for the automatic determination of the ventricular gradient in man Abstr 2nd World Congr Cardiol 15 274

7 GRANT R P & E H ESTES JR 1951 Spatial Vector Electrocardiography Blakiston Philadelphia Pa

8 KOSSMANN C E S A BRILLER & N MARCHAND 1955 Relative efficiency of depolarization and repolarization of the myocardium determined from the spatial vectorcardiogram Circulation Research 3 203

THE VENTRICULAR GRADIENT OF WILSON

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'It is the purpose of this article to describe a method of analyzing the electrocardiogram which has not been employed hitherto and which yields information not obtainable in other ways This is the opening line of the paper[1] that introduced the concept of the ventricular gradient entitled The Determination and the Significance of the Areas of the Ventricular Deflections of the Electrocardiogram Its authors were Frank N Wilson A Garrard Macleod Paul S Barker and Franklin D Johnston This paper in our opinion is unmatched in its field either in the logic of its development or its importance as a scientific achievement It seems however that no concept introduced into electrocardiographic thinking has been more neglected in spite of the fact that its further development by Ashman[2, 3, 4] and his associates and by Bayley[5] demonstrated its importance as a scientific and clinical tool in the interpretation of the recovery (T) potentials This is in part due to the fact that in some quarters the notion has become popular that concepts employing the vector method cannot yield correlations when the standard limb leads are used for the construction of the vectors It is the purpose of this presentation (1) to show that the concept of the ventricular gradient is an important scientific and clinical tool (2) to show that the effects of eccentricity contour and inhomogeneity do not completely destroy its usefulness, and (3) to discuss some of the implications of the concept with respect to certain attempts at spatial vector analysis

As Wilson described it the ventricular gradient is a measure of the electrical effects produced by local variations in the duration of the excitatory process ' Expressed as a vector quantity it gives the direction and magnitude of the electrical forces produced by a lack of uniformity in the duration of the excited state

A brief review of the concept of the gradient is presented in FIGURE 1 It is to be noted that if the duration of the excited state (rate of repolarization) is uniform throughout the muscle and the sequence of repolarization follows that of depolarization the QRS complex is followed by a T wave of equal area and of opposite sense for the quantitative potential change during depolarization and repolarization must be the same although in opposite direction Following Burdon Sanderson this diphasic curve is represented as the result of the algebraic addition of two oppositely directed monophasic curves each representing the curve produced (theoretically) by depolarization and repolarization of the opposite ends of a muscle fiber or opposing surfaces of a segment

The Cardiac Research Laboratory of the Touro Infirmary is supported by grants from the John A Hartford Foundation New York N Y and the J Aaron Research Fund of the Touro Infirmary

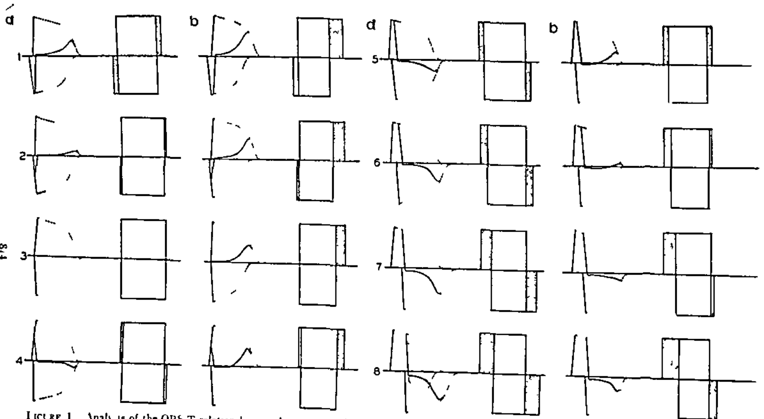


FIGURE 1 Analysis of the QRS T relationship employing monophasic curves. Series *a* represents the uniform duration of the excited state (the two monophasic curves are identical in duration and form). Note (as is clearest in the rectangular representation) that the area of T plus the area of QRS always equals zero no matter how the two curves are related with respect to time. Series *b* represents different durations of the excited state (the two monophasic curves are of different duration). Note that algebraic addition of the area of QRS plus the area of T is again constant no matter how the two curves are related with respect to time but that this constant *is not zero*. This quantity is the net electrical effect of the differences in rates of repolarization. It is the gradient effect. Diagram 3*b* represents the result when all the muscle is excited simultaneously. *The T wave that results in this instance is entirely due to gradient effects.*

of ventricular wall* If the duration of the excitatory process is uniform then for any fiber or segment of ventricular wall the duration of the two monophasic curves is identical and regardless of how the two curves are related in time (and regardless of which occurs first) the T wave will be of opposite direction and of area equal to that of the preceding QRS complex and the result of algebraic addition of the two areas (AQRS + T) will invariably be zero On the other hand if the duration of the excitatory state is less in one area this may be represented by decreasing the duration (and therefore the area) of the monophasic curve for that region Under these circumstances the result of algebraic addition of the areas of the QRS and T complexes will again invariably be the same regardless of how the two monophasic curves are related with respect to time *but it will not be zero* This residual quantity is a measure of the net electrical effect of the difference in the duration of the excitatory state in the areas of muscle under consideration This area (AQRST) may be measured in any two limb leads and may be plotted on the Einthoven triangle as a vector quantity the *manifest gradient vector* When the complexes are recorded from the heart the areas that result actually represent the addition of a multitude of paired monophasic curves in various orientations If the T wave and the QRS areas are plotted in the same manner the mean frontal plane T and QRS vectors are obtained and the gradient vector is of course the resultant of these two vectors quantities according to the law of the parallelogram of forces

These frontal plane vector quantities may be regarded as the projections of spatial vectors For the normal heart Ashman *et al*[2] estimated that the mean spatial QRS vector was at an angle of 90 to the longitudinal axis of the heart and that the spatial gradient vector lies between these two in approximately the same plane as that of the QRS loop making an angle of 30 with the mean QRS vector (FIGURE 2) At the very outset it was emphasized by Wilson[1] by Bayley[5] and by us that *it is the relationship of the magnitude and direction* (especially the latter) *of the ventricular gradient to the magnitude and direction of the mean QRS vector which is important* Neither the magnitude nor the direction of the gradient has much meaning except in relation to the mean QRS

As shown in FIGURE 3 the frontal plane gradient usually lies to the right of the mean QRS in counterclockwise hearts and it lies to the left of the mean QRS in the hearts that are rotated clockwise about the anatomic axis Thus the QRS loop is the only available key to the proper relationship of the gradient vector to the AQRS vector Aid in determining the orientation of the system of vectors that we employ is obtained by use of the idealized normal QRS loop shown in the figures This loop had its origin in inferences drawn from the hypothesis of the path of accession formulated by Gardberg and Ashman[6] in 1943 and owes its present form to Ashman who altered the loop shown in that article by trial and error until he found the form that accorded best with most of the frontal plane loops that he painstakingly constructed from the limb leads of hundreds of normal persons

* It is accepted that for a segment of ventricular wall the sum of the total effects is equal to the sum of the opposing effects of the endocardial and epicardial surfaces All interior effects cancel out

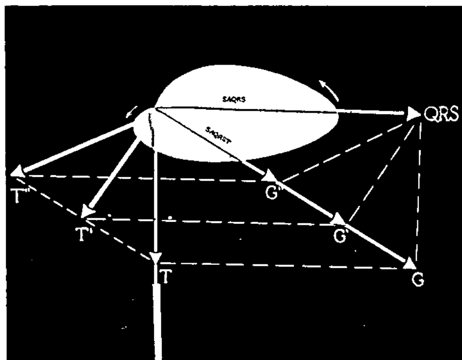


FIGURE 2 The idealized spatial QRS loop is shown lying in the plane of the page and not in an anatomical position The mean spatial QRS axis (QRS) is shown lying at 90 to the longitudinal axis of rotation (H) and the spatial gradient vector (G) is shown lying at a 30 angle to the mean spatial QRS axis all lying in the plane of the QRS loop The entire representation is idealized but some variations of course occur (see text) The spatial T vector (T) at rest is usually close to the longitudinal axis (H) Progressive diminution of the magnitude of the gradient (G) from such causes as increased rate exercise food or digitalis progressively produces T vectors T and T This model may now be employed to represent almost the entire range of variations of the normal electrocardiogram under a variety of non pathologic conditions

There are those[7] who would object to an idealized general form for the normal QRS loop on the ground that loops electronically recorded in various laboratories have a great variety of patterns that defy any attempt at stereotyping The implication that because the loop is recorded with electronic equipment it is thereby imbued with some unassailable quality is rejected for reasons too obvious to mention Furthermore we have proven that such stereotyping is possible for the frontal plane projection This alone makes it necessary that the spatial loop have some general form whether it can be recorded or not Finally on philosophical grounds one must object to the notion that the spatial QRS loop behaves differently from all other biological characteristics that follow a normal distribution curve (excepting sex) Thus we predict that when an accurate orthogonal system has been found a general form of the normal QRS loop (including timing) will be evident Indeed this will be our first requirement before accepting it

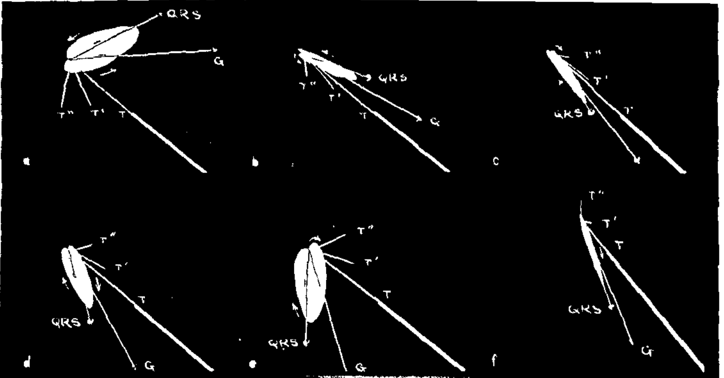


FIGURE 3 The loop vector system of FIGURE 2 shown in 5 (*a b c d* and *e*) orientations that result from rotation about the longitudinal axis (H) and one special orientation (*f*) Note that in the *counterclockwise hearts* (*a* and *b*) *the frontal plane gradient lies to the right of the frontal plane* QRS and that in clockwise hearts the frontal plane gradient lies to the left of the frontal plane mean QRS Note also that if the analysis holds factors that diminish the magnitude of the gradient should cause (1) rightward deviation of the T axis (T T) in counterclockwise hearts (2) leftward deviation of the T axis (T T) in clockwise hearts (*3*) *no deviation* if the loop is viewed on edge the magnitude of T *simply becoming smaller* and (*4*) *that if a* subject can be found whose loop is in position *f* diminution of the magnitude of the gradient might cause T to change to T resulting in inversion of the previously upright T waves in all three limb leads

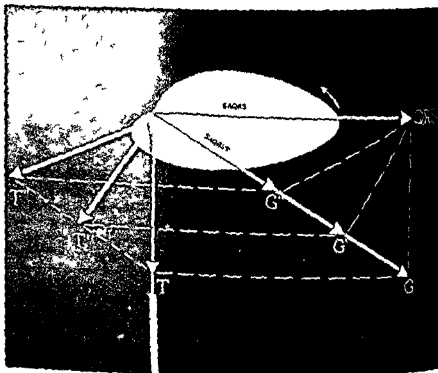


FIGURE 1. The idealized spatial QRS loop is shown lying in the plane of the page and not in an anatomical position. The mean spatial QRS axis (QRS) is shown lying at 90° to the longitudinal axis of rotation (H), and the spatial gradient vector (G) is shown lying at a 0 angle to the mean spatial QRS axis, all lying in the plane of the QRS loop. The entire representation is idealized but some variations of course occur (see text). The spatial T vector (T) at rest is usually close to the longitudinal axis (H). Progressive diminution of the magnitude of the gradient (G) from such causes as increased rate, exercise, food or digitalis progressively produces T vectors T and T. This model may now be employed to represent almost the entire range of variations of the normal electrocardiogram under a variety of non-pathologic conditions.

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Magnitude of the Gradient

As measured in individual tracings the magnitude of the gradient can be interpreted only with great caution because it varies with a variety of nonpathological factors even in the same individual. Increased rate, digitalis, exercise, food and smoking are among the factors that diminish the magnitude of the ventricular gradient. In the system developed in FIGURE 2 it is seen that if the mean QRS remains unchanged, progressive diminution of the ventricular gradient causes the direction of the mean T axis to deviate away from the direction of the mean QRS vector and that the locus of the tip of the mean T axis during this change is a straight line drawn through the tip of the original T axis parallel to the direction of the ventricular gradient vector. FIGURE 3 illustrates the same model photographed in various rotations about the longitudinal axis. It leads one to expect that in the counterclockwise heart those factors that diminish the magnitude of the gradient will cause the mean T axis to deviate to the right, that in clockwise hearts the same factors will cause the mean T axis to deviate to the left, and that in hearts whose orientation is such that the loop is viewed on edge, the T axis will not change in direction but will simply become diminished in magnitude. Furthermore, if we place the model in the position shown as *f* in FIGURE 3 we can see that theoretically it may be possible to invert the previously upright T waves of all three standard limb leads by diminishing the magnitude of the ventricular gradient. One need only find a subject whose loop is oriented as in *f* of FIGURE 3.

In FIGURE 4 we see on the left the records made before and after exercise of a young healthy male with a counterclockwise heart (see oscilloscopic frontal plane loop). Here it is seen that the most notable change is a diminution of the magnitude of the gradient and a consequent deviation of the mean T axis to the right. T_I becomes lower and T_{III}, previously inverted, becomes upright.* If the T axis deviates further to the right, T in aV_L becomes inverted (FIGURE 5). In the center of FIGURE 4 are the observations from a subject with a heart in an orientation such that the loop is viewed almost on edge. Here it is noticed that exercise again causes a diminution of the gradient and, as was expected, the mean T axis does not change materially in direction but is reduced in magnitude. The data of the subject with clockwise rotation of the heart are shown on the right. Here again exercise reduces the magnitude of the gradient and, as expected from FIGURE 3, the mean T axis is deviated to the left. As a result, T_I becomes slightly smaller and T_{III}, previously upright, becomes inverted. In FIGURE 6 are shown the observations on a subject whose QRS loop (q.v.) corresponds closely to the orientation of the model loop shown in FIGURE 3f, reproduced here. Again exercise diminished the magnitude of the gradient and resulted in the change in the T axis shown in the photograph of the model. The tracings show a sharp inversion of the T waves in leads II and III and a small inverted T wave in the first two complexes of lead I. FIG-

* These observations were made under controlled conditions. The subjects were fasting. The exercise was 20 deep knee bends performed rapidly. The 3 standard limb leads were made simultaneously with a polychannel apparatus operated at paper speed of 50 mm./sec. The areas of the complexes were measured from a carefully drawn base line without the use of other apparatus. No correction in area measurement was permitted once plotting had begun.

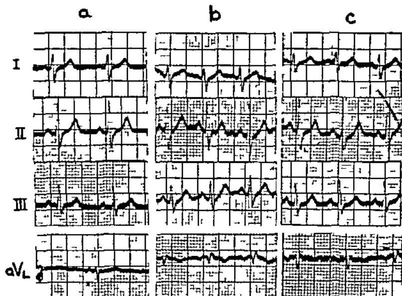


FIGURE 5 Tracings before and after exercise of a 20 year old youth with an apex back counterclockwise heart Note the inversion of T in aV_L

URE 5 shows a counterclockwise heart in which the rightward deviation of the T axis is sufficient to invert the T wave in aV_L

It should now be obvious that the T deflections vary greatly and in a most confusing manner in the absence of disease and that order is brought to this chaotic state of affairs only by employing the concept of the gradient A variety of nonpathologic factors diminishes the magnitude of the gradient The T deflections simply follow this rule as shown above

In most of the experiments described above the strikingly simple correspondence of the actual observations to the theoretical principles embodied in the model in FIGURE 2 is due to the fact that the QRS loop retained approximately the same orientation after the exercise as it had before This is not always true Very frequently the heart becomes more vertical after exercise as a result of the higher respiratory mid position and clockwise (less often counterclockwise) rotation occurs This is made evident by the changes in the frontal plane loop (and complexes) At times the effect of making the heart more vertical opposes the effect of gradient diminution upon the change of direction of the frontal plane mean T axis For example in FIGURE 7 the positional change *d* to *h* causes the manifest T axis to deviate to the right while diminution of the magnitude of the gradient causes this axis to deviate to the left Sometimes one effect predominates and sometimes the other gains ascendancy It is therefore important to relate the vectors to the loop which remains the only guide to normal QRS gradient vector relationship

Examination of FIGURE 7 representing the loop-vector system in a wide range of orientations shows the following conditions

(1) Measurement of the magnitude of the gradient in a large number of

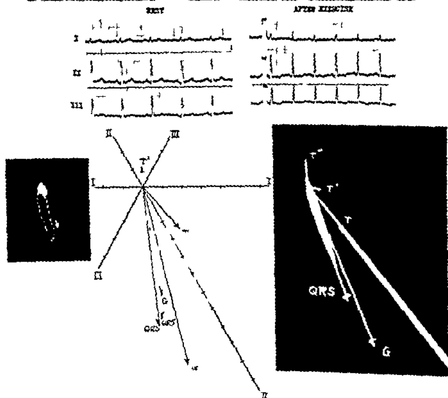


FIGURE 6 Results of an exercise test on a subject whose loop corresponds to that of FIGURE 3f Note that the observed T axis directions correspond to those predicted and that the T axes have become inverted in all of the three standard limb leads This is a perfectly healthy young man

normal individuals should give an extremely wide range of variation if we cover a wide distribution of heart positions and rotations The direction of the gradient also varies tremendously Statistical comparison of such a wide variation of values to a similarly wide range of values for the magnitude and direction of the gradient in all kinds of abnormal hearts is fruitless because in the latter group the magnitude and direction of the gradient can be greater or smaller than normal depending upon a variety of factors Only in congestive heart failure does the gradient almost invariably diminish in magnitude

(2) Graphic correlation on rectangular coordinate between the magnitudes of the manifest T vector and the manifest QRS vectors is *not* to be expected if a wide distribution of cardiac positions is covered

(3) In a large group of subjects of wide distribution of cardiac position graphic correlation between the components of the manifest T and manifest QRS on any one lead is not to be expected because the gradient varies so widely in direction and magnitude

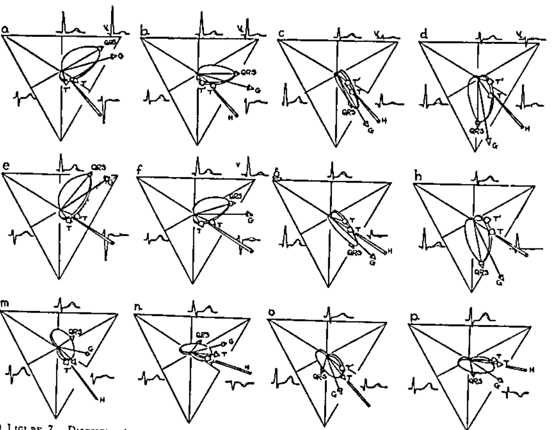


FIGURE 7 Diagrammatic representation of a wide distribution of orientations of the normal loop vector system

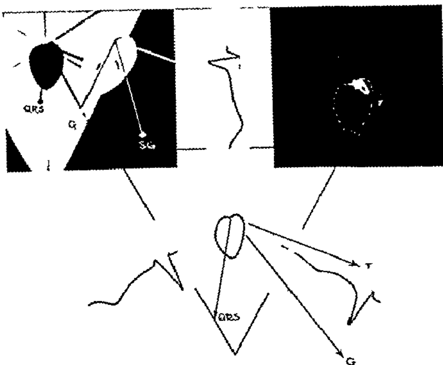


FIGURE 8 Estimation of the direction of the normal human ventricular gradient in the individual subject The line drawing shows the construction of the frontal plane loop from the limb leads and the calculated frontal plane mean QRS and gradient vectors The photograph at the upper right is the oscilloscopic frontal plane loop The photograph at the upper left shows the model loop vector system oriented in space so that a source of parallel light throws a shadow such that the form of the plotted loop and the direction of the mean QRS are both matched as closely as possible In this case the error in the actual calculated direction of the frontal plane gradient when compared to the direction of the shadow of the gradient on the photograph at the uppe left is about 6

The application of such attempts at correlation to the question of the validity of the concept of the gradient can be due only to misconception at a fundamental level Furthermore the notion that all relationships can be expressed in rectangular coordinates is obviously false

Frontal Plane Ventricular-Gradient Vector

Examination of the direction of the frontal plane ventricular gradient vector of the individual subject is presently being carried out in the following manner the orientation of the model loop shown in FIGURE 2 is found When this is projected on the frontal plane it matches the frontal plane loop constructed from the limb leads (or by oscilloscope)* The direction of the mean QRS

* The difference between loops constructed from the limb leads and those constructed by the oscilloscope is small in most instances

vector is also matched The frontal plane projection of the spatial gradient vector of the model loop now gives the predicted direction of the ventricular gradient (FIGURE 8) The measured direction of the gradient (plotted from the limb leads) is now compared with the predicted direction When this is done the error is small in many normals, but in others it is rather large although we are presently engaged in reinvestigation of this problem by the revised method just described and it promises to produce better results

Interestingly enough the measured gradient direction when it does not correspond closely to the predicted direction usually lies to the left of the predicted direction In such cases it appears that the gradient vector (and therefore the mean T vector) lies outside of the plane of the QRS loop (FIGURE 11) It must be significant that when this occurs (in normals) the vectors most often lie in a plane that is to the left of that of the QRS loop While this does not prevent the systematic behavior of the QRS T vector relationship as expressed by the concept of the ventricular gradient it does create several problems The first problem is represented by the wide latitude to the left that must be allowed in prediction of the direction of the frontal plane projection of the gradient in the individual case Closer examination may make it possible to know in which cases this latitude may be permitted and in which cases it may not be permitted The widest latitude should probably be permitted for the subjects with the narrowest frontal plane loops and apex

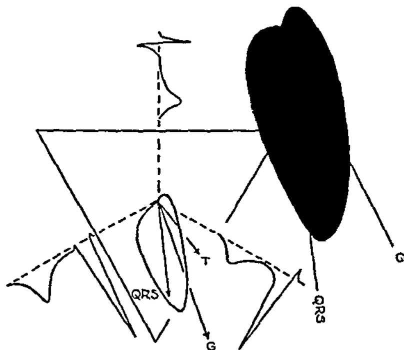


FIGURE 9 Example in which the direction of the gradient is predicted according to the method shown in FIGURE 8

back positions It seems probable that this problem is related to the eccentricity contour effects For example narrow loops at an axis of 80 to 90° (FIGURE 11) are probably often the result of distortion by eccentricity contour effects Ernest Frank found that anterior displacement of the dipole caused such narrowing of the loop as well as further clockwise deviation of its general direction The T loop need not undergo as much eccentricity change however (even if the same dipole location can be employed for QRS and T potentials) for the error in the direction of a manifest vector produced by eccentricity-contour effects is dependent among other things upon the direction of the dipole axis If the narrow loop is regarded as if it were viewed on edge (and it is so regarded) the gradient will be found to lie to the left of the expected direction Furthermore manifest QRS loops having a mean axis of 0 to 30° are frequently much distorted Here again is a group in which the T axis frequently lies out of the plane of the QRS loop This is the range of directions in which the eccentricity-contour effects are critical for dipole direction

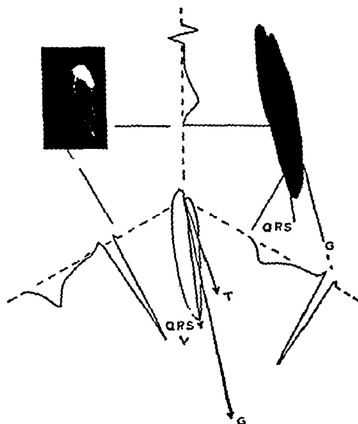


FIGURE 10 Example in which the direction of the gradient is predicted according to the method shown in FIGURE 8

in that dipoles of small difference in direction may produce manifest vectors of widely different direction For one, the error in direction may be clockwise, for the other, it may be counterclockwise This may occur for different parts of the QRS loop thus exaggerating minor irregularities and producing varying results as far as the mean QRS vector is concerned The T loop, usually containing vectors of narrow range of directions is more apt to be deviated as a whole

Records made with a more accurate system will serve to verify or to nullify these deductions

Rotations of the Heart

We have always realized that the cardiac rotations as employed in our analysis of electrocardiograms are quantitatively improbable The degree to which one must rotate the heart about the longitudinal axis to obtain the orientations of the QRS loop and vector axes that we have employed is exaggerated It seems hardly questionable that much of the exaggeration of the

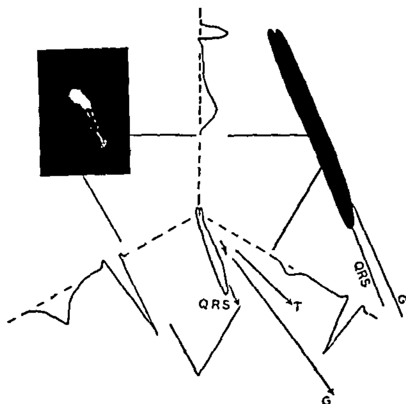


FIGURE 11 Example in which the direction of the gradient is predicted according to the method shown in FIGURE 8 In contrast to the examples shown in FIGURES 9 and 10 the error in this figure is large It represents an example of those cases in which the gradient is out of the plane of the QRS loop This may be accounted for in part by the eccentricity effect The notion that we believe that the gradient is necessarily precisely in the plane of the QRS loop in every case however is false

rotations as reflected in the loops and vectors plotted from limb potentials is accounted for by eccentricity contour effects Whether one employs the Burger triangle the experimental results of Ernest Frank, or the simple and possibly naive calculations of eccentricity effects alone as published by Gardberg[8] the results are similar (although quantitatively different) an even distribution of vector directions is spread over a much greater range of directions by these effects The effect upon frontal plane QRS loops will be similar Loops from counterclockwise hearts will appear more counterclockwise than they really are and loops from clockwise hearts will appear to be more clockwise than they actually are Furthermore the closing of the loop that occurs after exercise and with a deep breath probably is due in many subjects partly to a change in eccentricity effects and the suggested rotations about the vertical and anteroposterior axes are also exaggerated by the same factors One should expect to find however that the error itself is rather systematic, and experience shows that this must be true in the main for such correlations of which the foregoing examples are only samples would not otherwise have been possible

We do not for a moment doubt that it is desirable to find a method of recording the true direction and magnitude of the vectors that represent cardiac potentials if it can be done but it is impossible to subscribe to the notion that all electrocardiography has been and is empirical until such a method has been found Analyses of QRS loops and of QRS T relations in normal hearts in ventricular hypertrophies in infarctions in various locations and in right and left bundle branch block have been carried out within the Einthoven frame of reference and have been of great value[9] If a method is found that permits recording of the true magnitude and direction of the cardiac potentials it may be possible to refine these analyses further this of course is highly desirable We shall know that such a method has been found when it has been shown that similar spatial loops (including timing) are recorded from a large proportion of a significant number of normal persons whose loops are in a variety of orientations and if the relationship between the mean T and mean QRS vectors determined by that method are found to follow a general order in normals We believe that this order will be expressed by the ventricular gradient in the manner described above and that the QRS loop will be the guide to the spatial orientation of these vectors It should also be noted that if (as we suspect) examination with a more accurate system shows that it is difficult to correlate what we have called the longitudinal axis with X ray examination of the heart this will not affect the analysis It is the orientation of the loop vector system that is important to the analysis and not the manner in which it attained that orientation In the meantime as new developments in the knowledge of contour eccentricity effects occur it may be possible to apply them to better understanding of some of the phenomena that have been observed when the Einthoven method has been employed

Contour Eccentricity Effects in Relation to Gradient Analysis

Our theoretical discussion of the quantitative relationship of the QRS and T potentials reaches the conclusion that it is the relationship between the

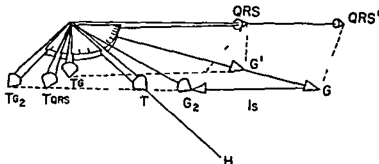


FIGURE 12. Widening of the spatial QRS T angle by three significantly different factors.

direction and magnitude of the ventricular gradient and the direction and magnitude of the mean QRS that is important. As such the T potentials are virtually meaningless. When we come to consider the contour eccentricity effects however it is necessary to realize that it is the T potentials and QRS potentials that are actually recorded and that the gradient is obtained by calculation. Undoubtedly the eccentricity contour effects frequently cause exaggeration of the widening of the angle between the mean QRS and the mean T vector that occurs when the magnitude of the gradient is diminished. In such cases the gradient will appear to diminish to a greater extent than it actually does. It is equally apparent that at times the same effects minimize this same angle and that the gradient will appear to diminish less than it actually does.* Partly for this reason, quantitatively similar effects of exercise for example are not found in different individuals. It may be that soon when an accurate method of measuring spatial vectors is achieved more uniform results will be obtained.

Evaluation of the Spatial Angle Between the Mean QRS and Mean T Axis

We have already shown both theoretically and experimentally that the spatial angle between the mean QRS and the mean T vectors is widened by nonpathologic factors and that this is the result of diminution of the magnitude of the ventricular gradient. It is important to point out that if the mean QRS shown in FIGURE 12 increases from QRS to QRS (as in left ventricular hypertrophy or in delayed conduction in the left bundle branch) the angle between the mean QRS and the mean T must become greater (secondary T axis change) unless the gradient changes in direction or magnitude. Furthermore if ischemia develops in such a location that its electrical effects may be represented by the vector *Is* in FIGURE 12 the angle between the mean T vector and the mean QRS becomes wider in a fashion not strikingly dissimilar to that which resulted from nonpathologic factors. Thus we have very similar widening of the spatial QRS T angle due to extremely similar changes in the T vector direction that result from three significantly different factors. Superficial

* This will be true even if single dipole representation is proper and even if the same dipole location may be employed for the T as for the QRS potentials and if contour-eccentricity effects differ with dipole direction.

examination fails to reveal these factors They can be distinguished only in terms of the ventricular gradient as the expression of the quantitative relationship of the mean QRS and T values One change results from diminution of the magnitude of the gradient the second results from increase in the mean QRS due to left ventricular hypertrophy or left bundle branch block (while the gradient remains unchanged in magnitude and direction), and the third results from a change in the direction of the ventricular gradient due to myocardial ischemia

Since the spatial angle between the mean spatial T axis and the mean spatial QRS axis has no specific meaning a warning is issued to those who employ this method of analysis without considering the nonpathologic factors that affect the magnitude of the gradient and without using gradient analysis of secondary T axis changes Of course a correlation of the magnitude of the spatial T with the spatial QRS may be found in normals if the subjects are examined under basal conditions and in these there may be some constancy of the spatial angle between the spatial vectors QRS and T

FIGURE 13 shows two of the many clinical applications of the concept of the gradient In the upper vectorial representation QRS G and T are the normal mean spatial QRS gradient and T vectors respectively When left ventricular hypertrophy occurs QRS increases to QRS , and the mean spatial T axis becomes T If the patient is then digitalized the gradient is diminished to G_1 and T now becomes T_2 The corresponding changes that occur in the limb leads are shown (in order) in the left hand set of drawings of leads I II and III The actual set of tracings reproduced in the figure are those before and after digitalization of a patient with left ventricular hypertrophy

In the lower vectorial representation of FIGURE 13 the same QRS G and T vectors are for the normal heart When posterior infarction occurs the QRS is caused to swing forward to QRS It may become longer or shorter depending upon whether the infarct extends into the septum or laterally The gradient direction is deviated upward and forward becoming G and the T vector therefore becomes T (primary T change) The fact that the vectors QRS G and T are in the same plane in this illustration is geometrically unavoidable The fact that this plane is perpendicular to the frontal plane in this illustration however is purely fortuitous and is not essential to the forthcoming result of the analysis If left ventricular hypertrophy now occurs QRS becomes QRS and T of necessity changes to T″ (secondary T axis change) The complexes that occur in leads I II and III with each of these changes are drawn in the upper right hand corner of the figure

Because of neglect of the principle of the gradient such secondary T wave changes are not recognized and erroneous interpretations are made

Frontal Plane versus Spatial Measurements

We have confined ourselves to frontal plane measurements Our spatial representations are obtained by inference from the frontal plane studies We have felt that any method of direct *spatial* vector measurement should yield important advantages to justify the use of the more complicated method

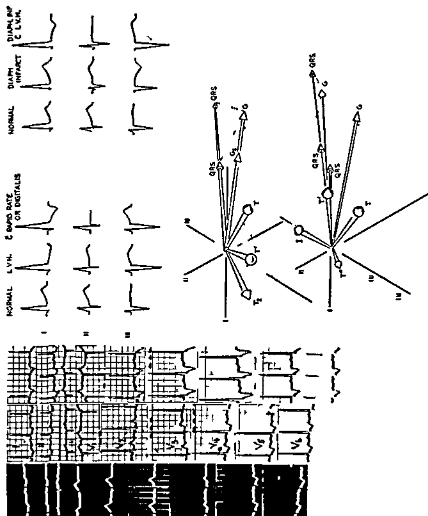

NORMAL
L.V.H.
C̄ RAPID RATE OR DIGITALIS
NORMAL
DIAPH. INFARCT
DIAPH. INF. C̄ L.V.H.
QRS
G
T

FIGURE 13

Furthermore we feel that the errors of the horizontal leads of the cube and tetrahedron are in general greater than those of the Einthoven method and that they are not as systematic The combination of two systematic errors unless they are correlated in some way will probably lead to confusion Time does not permit full discussion of this subject The orthogonal leads of Schmitt or the newer method of Frank may be satisfactory If so they will make it possible to refine the analyses described above It is to be hoped that caution will be exercised in arriving at this conclusion It seems to be necessary to point out that an accurate system must make it possible to observe QRS spatial loops of similar characteristics in different normal subjects and in the same subject under different nonpathologic conditions It must also have reasonable accuracy under conditions such as right ventricular hypertrophy bundle branch block and infarctions

When such a method is found the principles of analysis should be much as described above In some respects the results may be more refined but distinction between normal and abnormal may be less marked in some instances than those observed with the method presently employed

RS T Shifts and the Ventricular Gradient

This subject has been dealt with so clearly by Ashman[4] that only a short review is presented here

The diagram of FIGURE 1 shows that as the ventricular gradient diminishes especially when the QT interval is short (FIGURE 1 diagram a8) a shift of the RS T segment occurs Since the QT interval is shortest with rapid rate and digitalis these RS T shifts due to diminution of the magnitude of the gradient will be encountered most often under these conditions

It is clear from the diagram of FIGURE 1 that the RS T shift is due to the fact that repolarization in one area (for example the endocardial surface) has already produced detectable electrical effects before depolarization of the opposing area (epicardial surface) has become complete It is notable that of necessity the RS T shift due to gradient diminution is opposite in direction to the QRS If an R and S are present the shift is apt to be opposite to the direction of the deflection of the largest area As a rule if the areas of R and S are equal the RS T shift does not occur

Thus we arrive at the rule that *RS T shifts that are due to nonpathologic diminution of the magnitude of the gradient are generally opposite in direction to and proportionate in magnitude to the main deflection (in terms of area) of the QRS complex* Some exceptions may be noted in leads in which the component of the gradient is zero or negative

It is obvious that the empirical limitation of the magnitude of RS T shifts which may be normal without regard to the direction and magnitude of the QRS complex is erroneous

Summary

It has been established that the relationship of the magnitude and direction of the ventricular gradient vector to the direction and magnitude of the mean

QRS is important in the analysis of the ventricular recovery potentials The effect of various nonpathologic factors has been shown to result from a diminution of the magnitude of the ventricular gradient It has been shown that such diminution of the magnitude of the ventricular gradient causes an increase in the angle between the mean T axis and the mean QRS A similar increase in this angle results from an increase of the mean QRS (as in left bundle branch block and left ventricular hypertrophy) and also as a result of change in the direction of the ventricular gradient (as in ischemia) The three similar T vector deviations that widen the angle between the mean QRS vector and the T vector can be distinguished only by study of the relationship of the gradient vector to the mean QRS vector Of course it is to be noted that in ischemia and infarction the angle between the spatial gradient vector and the mean QRS vector may become larger or smaller than normal depending upon the location of the lesion Furthermore ischemia frequently causes the axis of the spatial gradient to deviate remarkably from the plane of the QRS loop

When infarction occurs the QRS loop and the gradient are both changed but not necessarily in a correspondingly quantitative manner because the bordering ischemic effects are not quantitatively related to the size of the area of necrosis and because there are frequently some locational differences (the ischemia does not necessarily surround the infarcted area in a regular manner) In such cases the gradient vector and the QRS loop may or may not be in the same plane In such instances the QRS loop itself is often doubled on itself Attempts to employ QRS loops that show effects of infarction as a guide to the relationship of the mean QRS to the spatial gradient as if they were normal loops are useless

RS T shifts commonly occur as a result of rapid rate excitement and exercise In such cases the shift tends to be opposite to the direction of the main deflection of the QRS complex according to the principle of the gradient Attempts to evaluate such shifts without relation to the QRS are erroneous

Employment of the concept of the ventricular gradient brings order to a variety of electrocardiographic phenomena that are otherwise without order and improves greatly the clinical interpretation of the electrocardiogram

References

1 WILSON F N A G MACLEOD I S BARKER & F D JOHNSTON 1934 The determination and the significance of the electrocardiogram Am Heart J 10 46

2 ASHMAN R M GARDBERG & F BYER 1943 The normal human ventricular gradient III The relation between the anatomic and electrical axes Am Heart J 26 473

3 ASHMAN R & F BYER 1943 The normal human ventricular gradient II Factors which affect its manifest area and its relationship to the manifest area of the QRS complex Am Heart J 25 36

4 ASHMAN R 1943 The normal human ventricular gradient The relationship between the magnitude A_{QRS} and G and deviations of the RS T segment Am Heart J 26 495

5 BAYLEY R H 1944 On certain applications of modern electrocardiographic theory to the interpretation of electrocardiograms which indicate myocardial disease Am Heart J 27 431

6 GARDBERG M & R ASHMAN 1943 The QRS complex of the electrocardiogram A M A Arch Internal Med 72 210

7 SIMONSON E O SCHMITT J DAHL D FRY & F BAKKEN 1954 Critique The

theoretical and experimental bases of the frontal plane ventricular gradient and its spatial counterpart Am Heart J 47 127

8 GARDBERG M 1954 A theoretic analysis of the effects of dipole eccentricity upon the manifest vectors the manifest QRS loops and the potential of the central terminal. Circulation 10 544

9 GARDBERG M 1957 Electrocardiography Hoeber Harper New York N Y

THE INTEGRATED ELECTROCARDIOGRAM

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Although rapid advances have been made in the understanding of the fundamental processes underlying the production of electrical energy by myocardial tissue and its subsequent distribution by the body clinical evaluation of the surface electrocardiogram remains largely a subjective discipline The purpose of this paper is to consider several measures of surface electrocardiograms that make possible a more objective evaluation

Since its introduction in 1931 by Wilson and his associates [1] the concept of the ventricular gradient has been explored sporadically Although a fair amount of data has been obtained concerning the frontal projection of this entity [2-5] little information has been gained with regard to the spatial magnitude and orientation of the ventricular gradient The tedium of the calculations involved probably has played a major role in delaying the gathering of these data

In order to circumvent this difficulty apparatus that enables the automatic computation of the ventricular gradient has been constructed The isosceles tetrahedral reference frame is utilized to obtain approximate orthogonal components of the electrocardiogram

Basically the apparatus consists of a three channel electronic integrator that is charged and discharged by high speed relays† activated at the appropriate time by a sequence of monostable multivibrators Instantaneous analysis of successive electrocardiographic cycles demands that the timing of the sequence be performed within each cycle The operation of the apparatus employed is diagramed in FIGURE 1 The P wave is utilized for synchronization by transforming its instant of rise into a sharp pulse by amplification clipping differentiation and the triggering of a blocking oscillator This pulse triggers a monostable multivibrator whose rectangular output is adjusted in length on a monitor oscilloscope to end at the initial ventricular deflection The rectangular wave is utilized to clamp the integrating base line to the potential present at the end of the P R interval and to discharge the integrator The trailing edge of this wave form triggers a second variable monostable multivibrator whose duration is adjusted by monitoring to coincide with the period of ventricular activity A permanent record of this latter rectangular wave is obtained superimposed on one orthogonal component This second rectangular output is utilized to (1) unblank a dual beam cathode ray tube so that the frontal and horizontal planar projections of the spatial vectorcardiogram may be recorded and (2) to connect the integrating circuits simultaneously to the electrically isolated output of the amplified orthogonal components A third rectangular wave of fixed length fired by the trailing edge of the preceding pulse activates a transfer relay that replaces the patient connections with

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† Spring wire relays type AI Bell Telephone Co

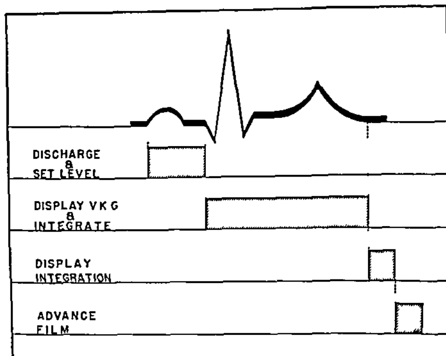


FIGURE 1 The sequential operation of the synchronization apparatus is represented by the relationship between the electrocardiogram and the shaded rectangles Each rectangle represents the output of the monostable multivibrator used to control the function designated The first two multivibrators have been adjusted so that integration may proceed during the QRST interval

the stored output of the integrators and displays the ventricular gradient as two directed lines on the cathode ray tube A final multivibrator in the chain advances the film in the camera in preparation for the next beat Data obtained for each electrocardiographic cycle consist of the frontal and horizontal projections of both the vectorcardiogram and a point the locus of which is determined by the magnitude and direction of the ventricular gradient (FIGURE 2) By adjusting the duration of integration to include only the QRS interval the mean amplitude and direction of QRS as well as the vectorcardiogram free of the T loop can be recorded

A simple RC circuit utilizing laboratory grade condensers is the basis of the integrator employed The circuit shown in FIGURE 3 is actually one half of a symmetrical circuit for each of the three channels Diodes selected silicon units are needed to permit algebraic addition of the signals obtained Although simple the theoretical accuracy of such an integrator for the values utilized (R = 2 2 megohms C = 0 5 μf) over the frequency range encountered within an average electrocardiogram is good The precision for sinusoidal components increases from 86 per cent at 1 cycle per second to more than 99 per cent for all components in excess of 10 5 cycles per second

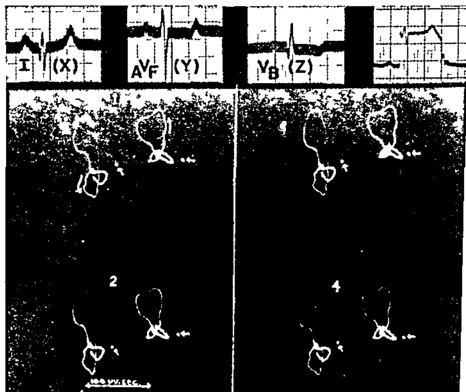


FIGURE 2 Four consecutive frontal and horizontal projections of the vectorcardiogram with similar projections of the ventricular gradient (points at the ends of the arrows) determined automatically are shown beneath the x, y and components of the electrocardiogram. To the right of the latter is a record of the y component displaced upward for an interval of time identical with the integration period.

Amplitude linearity was determined by feeding the apparatus rectangular pulses of approximately 0.16 sec. duration and varying in amplitude from 0 to 1 mv. The results (FIGURE 4) for each pair of channels demonstrate linearity of 90 per cent or better over the range tested.

A further critical requirement of this calculator is the ability to store an integrated output over a period of time. This aspect, loosely referred to as leakage, was tested by applying a 90 μv. sec. pulse to the computer. The integrated result was determined at intervals ranging up to 0.70 sec. after presentation of the problem (FIGURE 5). Deviations at the end of the specified time were 10 per cent or less of the initial value. It is to be noted that Q-T intervals greater than 0.50 sec. are rarely encountered.

Standardization of the apparatus was accomplished after each run by applying rectangular pulses of equal duration and of appropriate amplitude simultaneously to all channels. The length of the integrated result represents the radius of a 95 μv. sec. circle about the origin.

The averaged results obtained from a group of 10 normal young men were

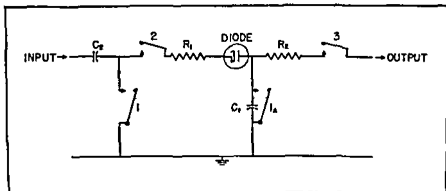


FIGURE 3 Schematic circuit of one half of the symmetrical integrator for one channel The relays symbolically indicated as switches close in the sequence of their numerical designation Relays 1 and 1_A which operate simultaneously discharge the network and establish the integration base line relay 2 determines the duration of integration and relay 3 permits observation of the integrated output Resistor R_1 is 2 2 megohms and R_2 is 10 megohms Condensers C and C_2 are 0 5 μf

compared with those from a group of 18 normal young men studied with an entirely different technique by Simonson *et al*[6] (TABLE 1) The elevation angles measured by these authors have been recalculated and expressed as the angle α_y The average normal direction of the spatial gradient is quite

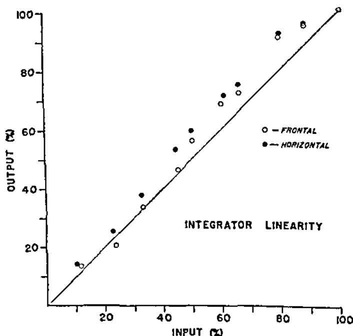


FIGURE 4 Integrator linearity

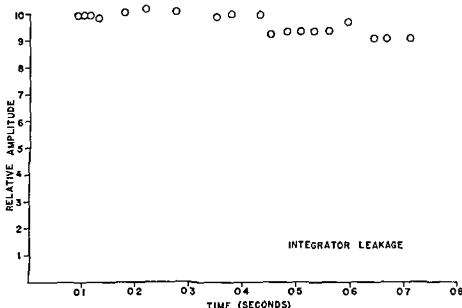


FIGURE 5 Integrator leakage

similar in both series The magnitude of the normal gradient is however 30 per cent smaller in the present series

These results were compared with 42 measurements obtained on 31 persons with various cardiac abnormalities (FIGURE 6) Nine follow up studies were obtained on 5 persons with acute myocardial infarction 4 posterior and 1 anterior The other etiological entities represented included most of the common cardiac abnormalities The ventricular gradients of individuals with heart disease tended to be randomly distributed in space and were less than 45 μv sec in both the frontal and horizontal projections The normal values with only one exception were of larger magnitude and they clearly tended to cluster in a left inferolateral spatial locus

It should be emphasized that although the data presented show a fairly clear separation of normals from abnormals the series is too small for examination by any sort of statistical analysis No selection of the study or control groups was made other than for the presence of a sinus rhythm, normal A V conduction and P waves of sufficient magnitude to be easily distinguishable from the inherent noise level at the time of recording

TABLE 1

	Area QRS			Area QRST		
	MAG μ sec	α y	α	MAG μ sec	α y	α
18 young men	42 8	34 9	−27 9	97 2	38 7	23 9
10 young men	38 8	32 9	−26 7	67 6	39 7	17 8

Although objective the ventricular gradient is by no means free of empiricism It has been stated that the gradient is an absolute expression of the differences in duration of the excited state of the endocardial and epicardial surfaces[2, 7] That this conclusion is justifiable only if the shape of the monophasic action potential measurable everywhere on these surfaces is identical in shape may be clarified by inspection of FIGURE 7 It can easily be seen that a change in velocity of the repolarization process at one surface may theoretically result in an upright T wave without a change in the duration of the excited state Although the sketch employed is a theoretical expression it should be pointed out that intracellular studies of the frog have demonstrated that a change in the velocity of repolarization occurs at least as frequently as does a change in the total duration of the excited state[8] Moreover it has been demonstrated recently[9] that endocardial versus epicardial velocity differences exist at least with respect to depolarization It is concluded that the ventricular gradient is an empirical measurement of the vectorial voltage residue measurable after one electrical systole and that as a first approximation it is present by virtue of differences in the time course of the excited state on the various analytical surfaces of the heart

In order to analyze the electrocardiogram by methods that yield results free of the vectorial notion of the gradient comparison was made of the surface

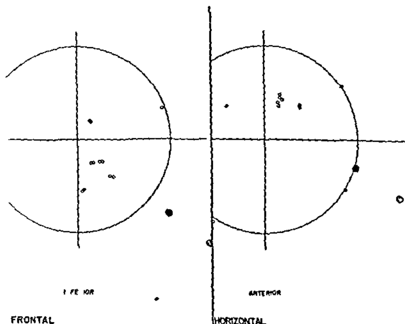


FIGURE 6 Frontal and horizontal projections of the ventricular gradient viewed from the front and from above respectively The open circles were obtained from individuals with heart disease the solid circles from normals The larger solid circles represent the average of the present series of normals and the crosshatched circles are the average of Simonson's normal series The large semicircles are the loci of a 50 μv sec area

forces of depolarization and repolarization as sums and ratios of manifest total voltage or voltage squared[10] Although the square of the voltage of depolarization expressed as a ratio of a similar measure of repolarization is an expression which may be regarded as an electrical work ratio it is clear that there is no implicit relationship between this ratio and the electrical work of the heart as a whole Despite interindividual differences of myocardial cells each cell must return to the same resting potential that preceded its active phase The total true depolarization/repolarization electrical work ratio of the heart were it measurable cell by cell would be 1 for any heart whatsoever

The *manifest* sums and ratios dealt with here are measured as follows spatial vectorcardiograms in two planes were obtained utilizing the isosceles tetrahedral reference frame The QRS and T loops were recorded separately and the magnitudes of the vectorial values of these loops at equal intervals of time (usually 0 0025 sec) were obtained by direct measurement after mathematically combining the two planes to obtain the spatial vectors at each instant These magnitudes were summed (where the voltage function was desired) or squared and then summed (where the manifest work ratio was desired) Multiplication by one half the time interval provided the desired data for QRS and for T *The results of such calculations are presented in*

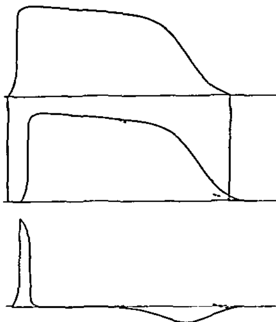


FIGURE 7 The lower diagram (solid outline) is the hypothetical electrocardiogram produced by stimulating a strip of muscle The upper figure is the monophasic action potential from a point at the stimulated end The middle figure is the monophasic action potential from a point most distant from the stimulated region If the time course of the excited state is identical at both regions (solid outline) a negative T wave will result in the lower figure obtained by subtracting the middle from the upper figure If the duration of the excited state remains fixed but the velocity of recovery changes at one site (dashed lines) an upright T wave will occur in the lower record

TABLE 2

P t e t	R ti s a d ms			
	$\frac{L_{Q\ S}}{L_T}$	$\frac{L_{Q\ S} + L_T}{2}$ (μ c)	$\frac{W_{Q\ S}}{W_T}$	$\frac{W_Q + W_T}{2}$ (m m)
E O C	3 75	138 70	23 98	288 55
A R	1 47	204 04	3 61	5,9 50
I G	0 64	248 18	1 07	740 10
J D	3 00	67 46	8 20	60 70
S L	0 31	66 00	0 59	38 16

TABLE 2 Sums and ratios of voltage ratios are prefixed by the letter L , whereas W designates an electric manifest work sum or ratio The five subjects for whom these entities were calculated were selected because their vectorcardiograms displayed large areas Such a prerequisite is necessary for accurate manual computation

Presumably the D/R energy ratio should be close to 1 In the normal sub ject (S L) it was 0 59 In patient I G it was 1 07 This 57 year old white widow had a strikingly abnormal electrocardiogram characterized by a high voltage of QRS and deeply inverted T waves in all of the usually recorded 12 leads except in leads III aV_R and V_1 Although she was regarded as having arteriosclerotic heart disease she was observed for 7 years without any change either in the electrocardiogram or in the normal size of the heart She has had no diminution of cardiac reserve but continues to have rather uncharacteristic pains in the chest to which the rubric anginal syndrome has been assigned as a result of conventional interpretation of the electrocardiograms In con trast the ratio in patient E O C was 23 98 Although his records were quite abnormal no clinical evidence of cardiac disease was apparent Three months after the special studies were done however he developed complete heart block with recurrent ventricular asystole and died within 3 days Patient A R and patient J D both with intraventricular block intermittent in the latter revealed values of 3 61 and 8 20 The first had cyanotic congenital heart disease The second had no clinical evidence of heart disease other than the block The ventricular gradient was measured in 2 of the 3 (I G and J D) and was abnormal in 1 (J D SG = 35 6 μv xy = 38 xz = −27) and normal in the other (I G SG = 69 7 μv xy = 70° xz = 28°)

It is impossible at this phase of investigation to assay the ultimate role of these data In a very preliminary sense the correlation of the D/R ratios with the clinical state of affairs in each case was good There is further appeal in these measurements since not being vectorial quantities they are dependent upon the configuration of the image surface of an individual but not upon the orientation of this surface relative to the anatomical coordinate system

References

1 WILSON F N A G MACLEOD & P S BARKER 1931 The T deflection of the elec trocardiogram Trans Assoc Am Physicians 46 29
2 WILSON F N A G MACLEOD P S BARKER & F D JOHNSTON 1934 The deter

mination and the significance of the areas of the ventricular deflections of the electrocardiogram Am Heart J 10 46
3 Ashman R E Byer & R H Bayley 1943 The normal human ventricular gradient. I Factors which affect its direction and its relation to the mean QRS axis Am Heart J 25 16
4 Ashman R F B P Ferguson A I Gremillion & E Byer 1945 The normal human ventricular gradient the relationship between AQRS and G and the potential variations of the body surface Am Heart J 29 697
5 Ashman R 1945 A statistical study of the ventricular gradient and of the QRS complex of the electrocardiogram Arch inst cardiol Méx 15 266
6 Simonson E O H Schmitt J Dahl D Fry & E E Bakken 1954 The theoretical and experimental bases of the frontal plane ventricular gradient and its spatial counterpart Am Heart J 47 122
7 Bayley R H 1955 Vector analysis of the T deflection of the electrocardiogram. Am Heart J 50 844
8 Kleinfeld M 1956 Personal communication
9 Scher A M A C Young A L Malmgren & R V Erickson 1955 Activation of the interventricular septum Circulation Research 3 56
10 Kossmann C E S A Briller & N Marchand 1955 Relative efficiency of depolarization and repolarization of the myocardium determined from the spatial vector cardiogram Circulation Research 3 203

THE PRESENTATION OF SPATIAL VECTORCARDIOGRAPHIC DATA ON A LINEAR TIME SCALE

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The studies I shall describe here are based on a consideration of the electrical events in the heart as arising from a dipole source and on the opinion that it is probably advantageous to record these events as vector quantities The display of these events as Lissajous figures has a serious disadvantage in that temporal relations are difficult to represent Several other methods of display are possible but the most straightforward technique appears to be one employing spherical coordinates With this system a vector is described in terms of its magnitude and two angles and these quantities can be displayed simultaneously as functions of time A computer that will permit direct registration of such traces has been constructed but records obtained by this means have not yet been analyzed Preliminary analyses of similar traces obtained indirectly from measurements of scalar ECG leads have been made The ECG leads were recorded with two systems of electrode placement on each subject One of these was the equilateral tetrahedron system and the other was based on the recommendations of McFee and Johnston[1,2] regarding electrode placement (FIGURE 1) X Y and Z components were recorded simultaneously and measurements of the magnitude of these components were made using a magnifying film reader that permitted measurements at intervals down to 0 003 sec The spatial magnitude the frontal plane angle through a range of 360 and the angle about an anteroposterior axis on a scale of -90 to $+90$ were calculated and these quantities were plotted as functions of time Thirty nine normal subjects and 18 subjects with a variety of ECG abnormalities were studied Analysis of these records has yielded the following results

(1) The information known to be clinically important in the conventional ECG is present in the new display in easily recognizable form

(2) There appears to be intrinsic merit in the presentation of VCG data on a linear time scale Variations of spatial magnitude indicated by notching of the QRS portions of these curves were not easily apparent in the scalar ECGs or in Lissajous figure displays of the VCG The possibility that this type of information might have clinical significance was indicated by the fact that there were larger notches in the curves of some subjects with myocardial infarction than there were in normal records This finding was present only in records obtained with the electrode system advised by McFee and Johnston

(3) Several measurements and methods of analysis that have limited meaning when applied to scalar ECGs and that are difficult to apply to Lissajous figure VCGs are appropriate to curves of the type described In the small group of magnitude curves studied to date there are statistically significant differences in the QRS width kurtosis and skewness of normal records and in those from subjects with myocardial infarction with both systems of electrode placement used With the McFee Johnston electrode system there is

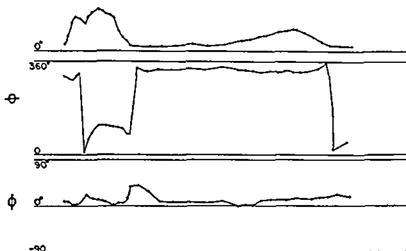


FIGURE 1 Linear time scale presentation of the spatial vectorcardiographic data These traces were derived from the measurements of the ECG leads of a subject with a posterior myocardial infarction The lead system used was the equilateral tetrahedron *R* represents the spatial magnitude of the cardiac vector as a function of time The angular deviations of the frontal plane projection of the cardiac vector are shown by Θ and are presented on a scale of 0 to 360 with 0 representing the left shoulder Orientation about an anteroposterior axis measured through a range of −90 to +90 with positive values directed posteriorly are shown by Φ

also a significant difference in the ratio of QRS and T areas in the magnitude curves of normal subjects and in those with infarction

(4) The wide variations in the spatial orientation of vectors representing the heart s electrical activity are reflected by the quantitative aspects of the traces indicating angular data but qualitatively these curves were easily categorized The QRS portions of the curves indicating angles in the frontal plane are simple monotonic functions or one of two varieties of inflected curves All curves of orientation about an anteroposterior axis are qualitatively similar

References

1 McFEE R & F D JOHNSTON 1953 Electrocardiographic leads I Introduction Circulation 8 554
2 McFEE R & F D JOHNSTON 1954 Electrocardiographic leads II Analysis Circulation 9 255
3 McFEE R & F D JOHNSTON 1954 Electrocardiographic leads III Synthesis Circulation 9 868

DISCUSSION PART III

C E Kossmann *Chairman*

A G MACLEOD (*The Upjohn Company Kalama oo Mich*) In connection with the frames of reference I believe that sometimes it is forgotten that in our original work we assumed that all leads were being taken at a very consider able distance from the heart itself and that consequently the moment one tries to get a spatial curve there is always one electrode that must be very much closer to the heart than another this will naturally introduce a consider able amount of distortion I feel that this accounts for the failure of these various reference systems to give the same angle between the QRS and T and the gradient We must be sure that we are dealing with lead points that are at a considerable distance from the heart itself for the analysis as originally used If we use a three dimensional vectorial analysis we are going to get into trouble For this reason I agree with Gardberg that we would do bet ter to stick pretty much to the frontal plane rather than try to locate the gra dient in space

O H SCHMITT (*University of Minnesota Minneapolis, Minn*) It has been said that the surest way to convert speculation into accepted fact is to give the speculation an attractive name I cannot help but wonder whether ventricular gradient would have been so frequently measured written about and used empirically in clinical practice had it been given a less imaginative less quantitative sounding name It is not my purpose to support or refute claims for the empirical utility of time integrated forms of the electrocardio gram Rather I should like to point out certain theoretical considerations that seriously limit practical measurement of the quantities idealized in these concepts

Wilson in forging the framework out of which these ideas have grown showed a remarkable intuitive foresight into the theory now commonly under stood and accepted by axonologists which states that a uniformly propagating nerve or muscle impulse leaves no first order external charge integral That is to say that except for irregularities in conduction such as those associated with acceleration tapering branching termination interaction fatigue and the like the externally measured action potential should integrate to zero over an entire cycle of activity

For a uniform single fiber this is almost exactly true experimentally as well as theoretically but for a whole heart measured via surface-derived leads variation in the registration of one part of the action current with respect to another is commonplace This is exaggerated in effect because the two principal complexes occur in the uncontracted and contracted states of the heart respectively thus giving full play to positional effect Rotation is also of considerable importance for a pair of exactly equal and opposite currents rotated as little as 60° with respect to one another leave a residual 100 per cent as great as either of the constituents

It must also be remembered that the normal electrocardiogram largely

represents even in the unintegrated form the cancellation of nearly symmetrical vectors We have only to observe the large and radically redirected resultant potentials accompanying pathway shifts or asymmetrical infarcts to realize that the integrated electrocardiogram is a difference of differences and hence a very sensitive but also a very erratic index of imbalance

Other factors of inadequately recognized influence upon the ventricular gradient are characteristic impedance variation tissue nonlinearity and local inhomogeneity Characteristic impedance is an electrical characteristic of a transmission line or physiological core conductor that depends upon the admittance and impedance of the fiber and surrounding tissue and that figures prominently in the determination of the distribution and intensity of currents during activity It also governs markedly the speed of propagation and the safety factor Adjacent fibers that fire simultaneously have a mutual effect on the characteristic impedance of one another and thus through nonlinearity well known to exist in the active membrane alter the propagation of the impulses in both

Tissue nonlinearity in its best known manifestation yields the rectification long ago demonstrated for nerve and now known to be of importance in all excitable tissues Currents generated in or near such nonlinear components do not obey the superposition theorem and so upon integration do not fulfill the basic conditions for cancellation

Tissue inhomogeneity is perhaps less important with respect to integrated potentials than nonlinearity but it certainly alters the registration of potentials intracyclically and further adds to the complexity of the interpretation of such recordings

Schmitt s table p 1106 shows that several different presumably orthogonal lead systems applied to the same person on the same day yield grossly different spatial directions in each system respectively for the QRS and T vector axes It might be argued that due to differences in weighting different lead systems will give somewhat different absolute directions and that furthermore QRS and T axes cannot be taken as representative of QRS and T time areas

To the second point one can answer that experimental measurement shows a remarkably close correlation in direction and magnitude between QRS and T time areas and their respective maximal vectors in normals and that the measurements in question were made on a carefully chosen typical normal

To the first point we can refer evidence regarding the *shift* of QRS and T direction and magnitude with respiration in the several lead systems The shift in axes and in magnitude is not even consistent in direction between the several systems and even the spatial angles between QRS and T vary inconsistently between systems From this I infer that only after the development of vastly improved lead systems can we hope to attain integral measures of sufficient internal significance to permit more than empirically valid interpretation

Consider next the theoretical implications of the recently developed techniques for potential squared time integration It would be admittedly very useful if we were able to devise a direct measure of the total electrical work expended in the action potential of the heart either on a simple scalar basis

or on a component basis vectorially related to the orientation of heart fibers. For the single isolated fiber measures of this energy have been worked out in line integral and in time integral form. For the whole heart however, these techniques are rendered useless by the nature of the integrals involved.

For the whole heart it is relatively easy to derive with a simple electronic computer the integral

$$S = \int_{\sim} \sum \left\{ \iiint_{V1} Z_a \, dM \right\}^2 dt$$

where Z is the transfer impedance vector and M is the current dipole moment density vector, the dot product of which is integrated throughout the heart volume. The resultant volume integral is squared and summed for the orthogonal directions α.

This is not the desired energy integral, however. The desired form is not even expressible in the form of a simple integral because energy is not summable in terms of dipole moment elements. Essentially, the difficulty lies in the difference between $a^2 + b^2 + c^2$ and $(a + b + c \quad)^2$, which are not even similar, especially when a, b and c can assume negative as well as positive values. We must then ask ourselves whether the above expression S has properties that might be empirically superior to those of a simple algebraic summation, vectorial or scalar, or an arithmetic sum.

An arithmetic summation differs from the squared form only in that large terms gain greater importance upon being squared. Algebraic vector summation is the familiar spatial vector ventricular gradient.

The only apparent advantage of the proposed quantity S is that it is presumably invariant with respect to orthogonal axis transformations. This is perhaps its principal justification.

Having made something of a case against the use of ventricular gradient, I should now like to point out that something very nearly identical to it can be measured by the use of very simple instrumentation.

If we recall that the function of a blocking condenser in our RC coupled amplifier is to reduce to zero the DC terms, then the potential on the far side of a blocking condenser unit integrates to zero over any long period and so gives a natural measurement of VG if an electronic look can be taken periodically at zero potential. This technique is automatically available *in the* SVEC II radial sheet modulator. Except for the shift area introduced by the P wave, this automatically points out the spatial VG.

E. Simonson (*University of Minnesota, Minneapolis, Minn.*) The concept of the ventricular gradient (VG) assumes a close relationship between QRS area and T area. More specifically, it assumes a negative correlation. Since the VG is defined as the algebraic sum of the QRS area and the T area, it can be constant only in case of a negative correlation, that is, if the QRS area increases the T area must decrease or become negative. This was actually demonstrated by Wilson *et al*[1] in one experiment on the heart of a dog. The heart was stimulated by means of electrical shock from various sites, resulting

in different directions and contours of the ventricular complexes The ventricular gradient was fairly constant, with a standard deviation of ±25 per cent of the mean The concept of the ventricular gradient was developed on the basis of this experiment

This experimental situation in the dog was quite different from the normal electrocardiographic routine in man, so that before any clinical application, the demonstration of a correlate in the normal human ECG to Wilson's experiment appeared to be important We were particularly interested in the interindividual correlation, because patients and normals can be differentiated only on this basis

Wilson s experiment, as well as the bulk of the VG literature is concerned only with the frontal plane QRS and T areas My associates and I[2] measured carefully the frontal plane QRS and T areas in 107 normal men by projection of the ECG's on a screen using Wilson s original method instead of Ashman's approximate and less accurate method No correlation was found between the frontal plane QRS and T area

We subdivided the total experimental sample into three groups according to the position of the QRS axis in the frontal plane and into three other positional groups according to the spatial orientation of the QRS and T vectors, we found no correlation between the QRS and T areas in any of these positional

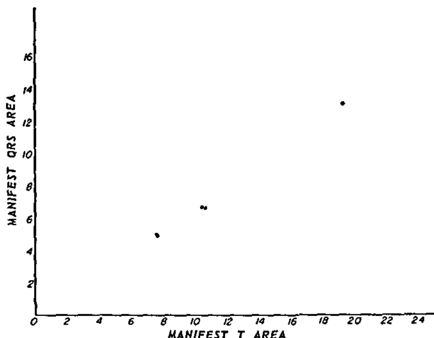


FIGURE 1 Lack of interindividual correlation between manifest T and QRS areas (frontal plane) The areas were measured with an electronic area integrator Reproduced with permission of the editor from the *American Heart Journal* 1954 vol 47 p 122 (F Simonson *et al*) figure 4C

groups We repeated the measurements with fifty men using an electronic area integrator in order to eliminate as far as possible the error of measurement as a cause for the lack of correlation Again there was no correlation (FIGURE 1) We cannot follow Gardberg in his argument that the absence of correlation should be expected If there is no correlation in normal population between the QRS and T frontal plane area, it is impossible to define any function in normal men comparable to Wilson s experiment in one dog Of course, a ventricular gradient can be numerically calculated but then a large scatter in normal population and an overlap with abnormal population should be expected This is actually the case, as found by various authors and also in our material

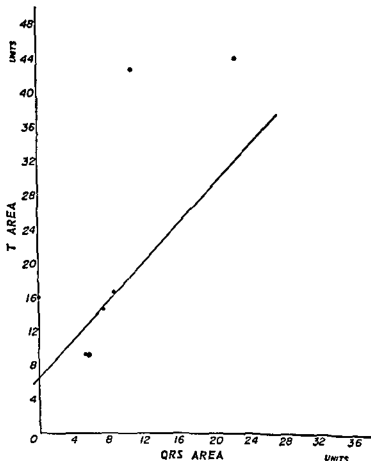


FIGURE 2 Significant positive correlation between spatial QRS and T areas According to the ventricular gradient concept a negative correlation should be expected Reproduced with permission of the editor from the *American Heart Journal* 1954 vol 47 p 122 (E Simonson *et al*) figure 7

The fact of a significant negative correlation in Wilson's experiment poses an interesting question. Is it possible that the VG is a function that has significance only in abnormal conditions such as those demonstrated in Wilson's experiment but not in the normal human ECG? In patients with left ventricular preponderance and strain, for instance, there seems to be a definite negative correlation between QRS and T with advancing involvement. As the R wave in lead 1 increases the T wave becomes more negative. In this connection it should be noted that Gardberg's material refers to patients. The main diagnostic value of the VG might well be in the follow up of the changes within individual patients rather than in the comparison of patients with a normal group.

We also measured the spatial QRS and T areas with a null point method using a mechanical vector analyzer[3] in combination with the electronic integrator. There was a highly significant correlation between the spatial QRS and

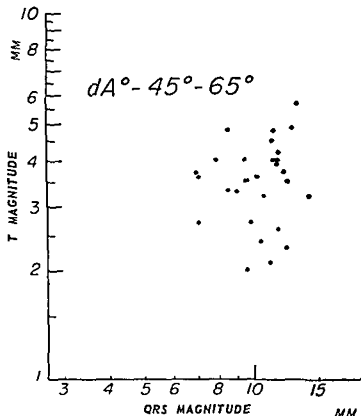


FIGURE 3. Scatter diagram (on a logarithmic scale) of the mean spatial QRS magnitude versus the T magnitude in 58 healthy men with an angle dA between the mean spatial QRS and T vectors from 45 to 65. There is a highly significant ($p < 0.001$) positive correlation. Republished from *Circulation* 1954 vol 9 p 105 (E. Simonson and A. Keys. The spatial QRS and T vector in 178 normal middle aged men) figure 1B (p 110) with permission of the publisher.

T area magnitude in eighteen normal subjects (FIGURE 2) but the correlation was positive and not negative as should have been expected on the basis of the ventricular gradient concept It should be noted however that the mean spatial QRS and T vectors also show a highly significant positive correlation (FIGURE 3)[4] This is not a coincidence because there is an excellent correlation between area and amplitude in any lead as shown in FIGURE 4 for lead I

In normal ECG s the area is fairly predictable from the amplitude and this is also true for many abnormal ECG s with smooth and symmetrical contours Due to the high correlation between areas and amplitudes abnormal deviations of area magnitudes and axes will correlate with abnormal deviations of mag nitudes and axes of spatial vectors as we have found in our abnormal material

The coefficient of variability (standard deviation in percentage of mean) was definitely smaller for the magnitude of mean spatial vectors than for the magnitude of spatial areas which shows that the consistency of the measure ments of spatial vectors is superior to that of areas

We arrived at the conclusion that the advantage that might conceivably be obtained in a few exceptional cases by area measurements does not justify the introduction of area measurements as a routine procedure in clinical electro- cardiography at the present time

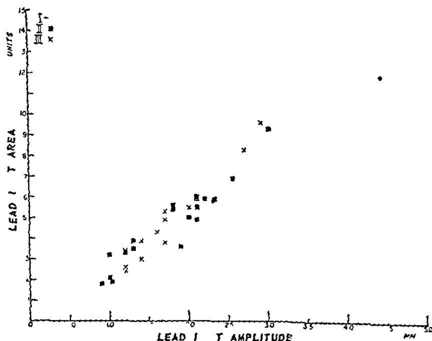


FIGURE 4 T_1 amplitude (abscissa) versus T area (ordinate) perfect correlation Repro duced with the permission of the editor from the *American Heart Journal* 1954 vol 47 p 122 (E Simonson *et al*) figure 8

References

1 WILSON F N A G MACLEOD, P S BARKER & F D JOHNSTON 1934 Am Heart J 10 46
2 SIMONSON E O H SCHMITT J DAHL D FRY & E E BAKKEN 1954 Am Heart J 47 122
3 SIMONSON E 1953 Circulation 7 403
4 SIMONSON E & A KEYS 1954 Circulation 9 105

RADIOELECTROCARDIOGRAPHY A NEW TECHNIQUE FOR CARDIOVASCULAR STUDIES*†

By Norman J Holter

Medical Physics Laboratory The Holter Research Foundation Inc Helena Mont

Introduction

The development of practical instruments for observing and recording electrocardiograms from human and animal subjects without the use of connecting wires between subject and recorder opens a new field for the investigation of some aspects of electrical phenomena accompanying cardiac activity The elimination of connecting wires (other than electrode leads) by the use of portable miniature equipment together with radio telemetering opens up possibilities for relatively long period continuous observation and/or recording of both normal and abnormal cardiac activity under conditions where electrocardiograms cannot be obtained with orthodox equipment Such conditions include exercise of various kinds and the physical and emotional conditions encountered in the stress and strain of daily living This technique which we have called radioelectrocardiography shows promise of providing a useful new tool to investigators in a number of physiological and medical fields

The development of radioelectrocardiography has been reported in scattered publications but to date has not been presented in a unified manner The field will therefore be concisely reviewed here and a brief progress report on the development of new auxiliary instruments at the Medical Physics Laboratory will be offered I should also like to raise some new questions that may be answered by the future use of this technique The subject is of necessity rather general at this time I hope that future use of this concept by workers in the biological sciences may contribute some new basic material to future publications on heart electrophysiology

None of us now knows what transient changes if any may occur in the electrocardiograms of a healthy cabinet member during the course of an all-day smoke filled conference on some international crisis For that matter what subclinical transient ischemic or other phenomena sufficient to affect ECGs might or might not occur during a day of normal heart activity?

The Development of Radioelectrocardiography

This field is relatively new Following some consideration of the rather limited and special conditions under which orthodox electrocardiograms were taken it was proposed that electrocardiographic studies be broadened both by an extension in time and by observations under conditions more realistic

* Funds for this study were contributed by the Holter Research Foundation Helena Mont

† Although not immediately concerned with the problems of excitation and recovery Mr Holter's article has been placed in this section because (1) it represents a new technique for the visualization of electrocardiographic changes under stressful conditions and (2) it may be considered to be a new venture in instrumentation and may thereby be related to the information presented by Briller and by Abildskov



FIGURE 1 Subject walking on the street during radioelectrocardiography—1 block from the laboratory

than those where the subject lies quietly in the electrocardiographic laboratory After some electronic development work the use of miniaturization and telemetering was shown to be feasible and information to this effect was demonstrated and published in 1949[1] as part of a more general project of broadcasting physiological data The name radioelectrocardiography provides equivalent terms for equipment and records The abbreviation RECG is convenient Further improvement of the equipment with additional results was reported in 1950[2] A combination of electrocardiography with broadcasting equipment was reported in Paris in 1950[4] but it is not known whether portability was intended Electronic details sufficient for construction of RECG equipment by others were published in 1952[5] Also in 1952 some preliminary tests were made on clinical subjects RECGs from a healed posterior myocardial infarction were obtained and compared with standard leads A note on this subject appeared in 1954[6] Electrocardiograms were reported broadcast from airplanes in 1954[7] as part of a study in aviation medicine The foregoing references are thought to constitute the complete bibliography in this field to date

Instrumentation for Radioelectrocardiography

Details of equipment are available in the literature cited The following is a brief description of the various units with brief mention of their intended use

The RECG transmitter FIGURE 1 shows one model of an RECG transmitter in operation with a human subject One of the small units seen fastened to the clothing is equivalent to the amplifier and power supply of an ordinary electrocardiograph and is connected to appropriate chest electrodes The other unit is the radio broadcasting and antenna system The units are small and light in weight and also can be mounted next to the skin beneath the clothing or carried in pockets Various harness and fastening arrangments can be used to fit special requirements The subject shown is broadcasting continuously to receiving equipment located in a laboratory one block away Nonstandard chest leads are used which prevent undue muscle interference during exercises such as trotting or deep knee bends

The RECG receiver FIGURE 2 illustrates a 1950 receiver model showing controls and an RECC pattern on the large long persistence oscilloscope screen The RECGs seen are being obtained from the subject pictured in FIGURE 1 The receiving antenna is shown mounted at the rear of the traveling cart The entire assembly can be rotated conveniently and moved about for best reception FIGURE 3 is a close view of a typical RECG during exercise It illustrates the general stability and nature of the trace The electrode positions are unorthodox Current work includes a study of the correlation between results from electrode positions needed by the RECC to minimize muscle interference under given conditions and those needed by the investigator in a given case

FIGURE 4 illustrates how normal activity can be undertaken by a subject during radioelectrocardiography This figure is a curve of continuous pulse rate versus time during the activities shown The RECGs were observed on

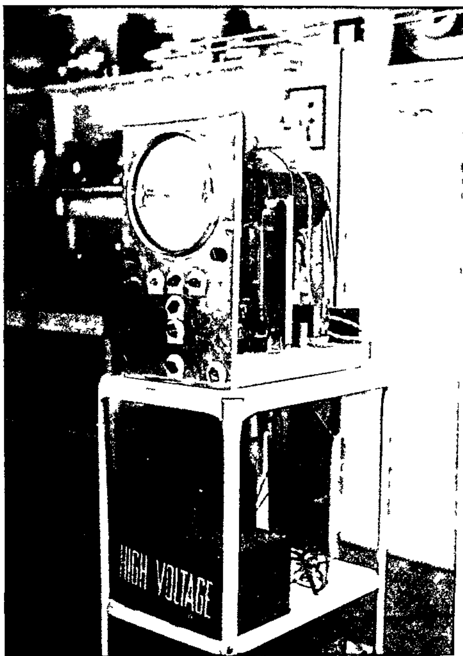


FIGURE 2 Early model of the RECG receiver showing the RECGs from the walking subject of FIGURE 1

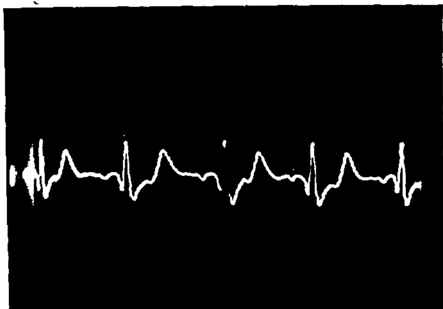


FIGURE 3 Close view of a typical RECG from an exercising subject nonstandard leads

an oscilloscope and they represent the second part of an experiment that began with a sleeping subject who arose dressed and then proceeded with the activity indicated in the figure

The portable RECG receiver recorder This instrument not illustrated is important in taking steps to give human subjects still more freedom for the realistic activity of daily living during radioelectrocardiography With the receiver unit of FIGURE 2 the subject must remain in the general environment of the laboratory Encouraging progress can be reported on the development of a miniature portable self powered receiver recorder unit to be carried by an experimental subject and kept in his immediate environment throughout the experimental period Something like a briefcase is now visualized to be kept in the office taken to a restaurant or left about the house continuously recording every RECG throughout the desired period Compactness is achieved by the use of magnetic recording on very thin tape 24 hours of RECGs (115 000 RECGs at a pulse of 80) being recordable on a reel 5 inches in diameter The RECGs would be identified temporally for use in correlating any anomalies with the circumstances that had occurred at the time such anomalies were recorded

Equipment for rapid reduction of RECG data The ability of the receiver recorder to provide continuous long period data naturally poses the practical problem of how to examine the voluminous records available from the tape recordings Work in progress has produced a promising semi automatic method for the rapid examination of radioelectrocardiography data For convenience

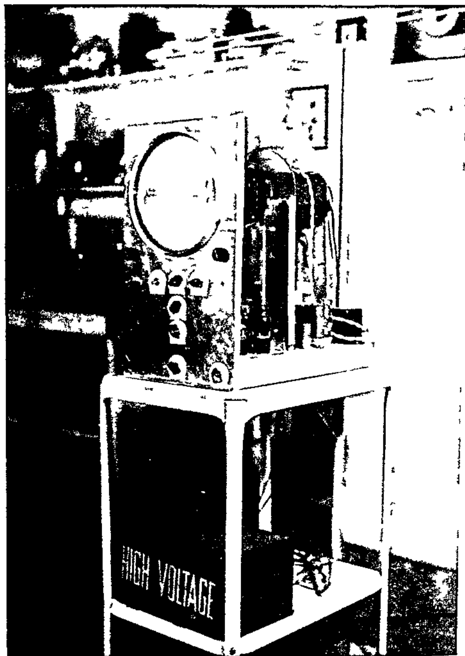


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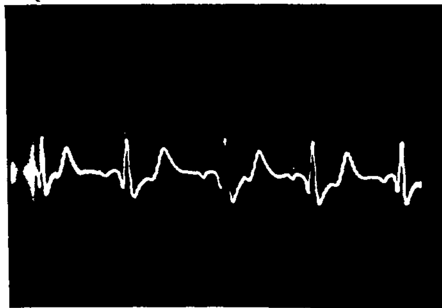


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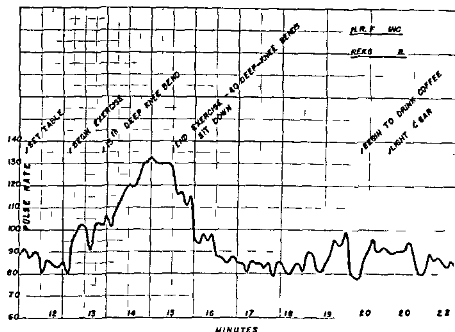


FIGURE 4 Continuous pulse rate record from a subject during exercise and ordinary activity (courtesy of McGraw Hill Publishing Co New York N Y)

in reference this method has been named the AVSEP method which is an abbreviation of Audio Visual Superimposed ECG Presentation so named for reasons that will become apparent With the AVSEP method 24 hours of continuous radioelectrocardiograms can be examined in less than 20 minutes to see which if any individual RECGs depart significantly from the norm When and if transient electrocardiographic changes are detected the observer can throw a switch to obtain orthodox paper ECGs from the tape for detailed examination

In the AVSEP method the magnetic tape records are played back at a rate about 80 times greater than that at which the recordings were made and the resulting signals are presented visually on an oscilloscope and at the same time audibly through a speaker The high rate of presentation for example 100 RECG/sec results in a rough growl on the speaker By synchronizing the horizontal oscilloscope sweep with the R wave of each RECG a steady pattern is seen on the screen each RECG being superimposed on its immediate predecessor to form a relatively steady pattern in spite of pulse rate variations

Any small change such as a depression of the T wave or elevation of the ST segment in even a few of the RECGs would be immediately apparent to the observer because of the transient change seen in the oscilloscope pattern accompanied by a transient change in the character of the sound presented by the speaker While transient changes are detectable either visually or audibly the combination appears to provide maximum resolution In tests made by

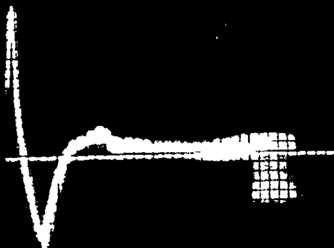


FIGURE 5 Photo of the AVSEP record of 800 successive superimposed RECGs Ten minutes of cardiac activity are presented for examination in 7 5 seconds This pattern is defined a normal for demonstrat on purposes

introducing artificial anomalies into tape records it has been found that transient RECG changes lasting as little as three heartbeats can be detected in the middle of a normal record It is believed that with improved equipment a single RECG departing from the norm will be detectable This would be significant in any study where highly transient changes might be sought such as in an investigation of what constitutes long period normalcy

A number of obvious electronic refinements remain to be added but the method apparently minimizes the data reduction problem It is applicable of course with minor changes to the study of records obtained directly at the bedside where long period recordings make it desirable

FIGURES 5 and 6 give an approximate idea of the appearance of the AVSEP pattern FIGURE 5 is a photograph of the AVSEP record of 800 successive RECGs This represents 10 minutes of actual heart activity presented to the observer in 7 5 seconds* FIGURE 6 shows another AVSEP record of about 600 RECGs in which the T wave has been modified by changing the electrode positions This is arbitrarily designated as an anomaly or cardiac episode when referred to FIGURE 5 defined as normal FIGURE 7 is the result

In all of these figures the signal has been uncorrected for the mathemat cal differentia tion inherent in the reproduction method Thi can be corrected by an integrating circuit Since the R wave trigge s the oscilloscope the P and Q waves are at the right where they are blurred by pul e variation Adjustable delay circuits are being constructed to allow presen tation beginn g with the P wave These figu es are for demonst ation purposes only

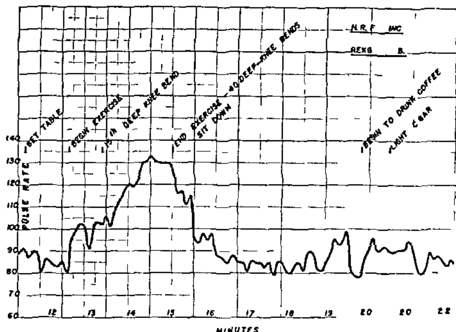


FIGURE 4 Continuous pulse rate record from a subject during exercise and ordinary activity (courtesy of McGraw Hill Publishing Co New York N Y)

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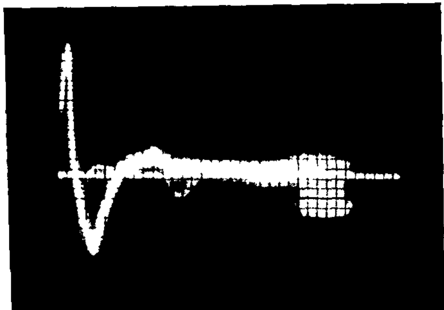


FIGURE 7 Photo of an AVSEP record demonstrating the appearance of transient anomalous RECGs Ten heartbeats of FIGURE 6 were introduced into the middle of 800 beats of FIGURE 5 and the whole was presented in 7 5 seconds The cardiac episode is readily detectable though lasting only 1/10 second in passing Resolution down to less than 3 successive anomalous RECGs appears possible Twenty four hours of continuous RECG record (over 100 000 individual RECGs) can be examined in less than 20 minutes by this method

than on the machinery which to some physicists is an end in itself I shall do no more here than merely raise some illustrative points As mentioned in the introduction orthodox electrocardiography has obvious limitations when physical activity is involved but it is not intended to imply that orthodox electrocardiography is overburdened with shortcomings One clinician has objected to radioelectrocardiography on the grounds that there is still so much to be learned and determined with present methods that adding the fourth dimension of time with the attendant complication of changing physiology (which can be pretty much ignored in arguing the merits of various lead systems in the light of a single heartbeat) is not in order However it is in the nature of science sometimes to find oneself working on the roof before the second floor is finished and this cannot be helped One would lack curiosity indeed if one were not tempted to see what electrocardiographic transients might exist in a normal man running to exhaustion or a woman in the throes of hysterics Consider the diagnostic and prognostic implications of answering the question At what step of the standard exercise test does the electrocardiogram first begin to change? as against answering the present question What is the difference between the electrocardiogram before and after the standard exercise test? Convenient studies of pulse changes during activity

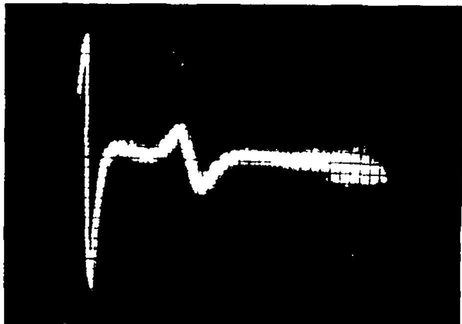


FIGURE 6 Photo of a record similar to that shown in FIGURE 5 but with the pattern artificially modified and defined with reference to the FIGURE 5 pattern as a cardiac episode for demonstration purposes

of a combination of the 2 previous signals with 10 heartbeats of FIGURE 6 recorded in the middle of 800 heartbeats of FIGURE 5 the pattern being photographed by exposure during the full play back time The cardiac 'episode' although lasting only one tenth of a second during AVSEP presentation is seen to be readily detectable Ten heartbeats were used to obtain sufficient photographic exposure Three or less can be detected by direct observation

Fortunately occasional transient radioelectromyograms and/or radio dead spots are detectable as such even though transient and they are readily *distinguishable from the transient changes resulting from true RECG changes* Thus the RECG AVSEP combination appears to remove many of the obstacles to the routine use of radioelectrocardiography in investigative and possible future clinical applications FIGURE 8 is a simplified block diagram of the over all operation indicating the basic units involved in radioelectrocardiography from the heartbeat to the detection of aberrant electrocardiographic activity Electronic details of the portable RECG receiver recorder and the semi automatic equipment for rapid data reduction my own and those of W R Glasscock will be presented elsewhere

Applications of Radioelectrocardiography

While this is primarily a report on the progress of an instrumentation idea it might not be out of order to keep our sights on some ultimate aims rather

References

1 HOLTER N J & J A GENGERELLI 1949 Remote recording of physiological data by radio Rocky Mountain Med J 46 749
2 WHITE P D 1951 Heart Disease 4th ed 182 Macmillan New York N Y
3 HOLTER N J & J A GENGERELLI 1950 A miniature amplifier transmitter for the broadcasting of bioelectric potentials 117th Ann Meeting Am Assoc Advance Sci Bull
4 WHITE P D 1951 Heart Disease 4th ed 225 Macmillan New York N Y
5 GLASSCOCK W R & N J HOLTER 1952 Radioelectroencephalograph for medical research Electronics 25 126
6 MACINNIS H F 1954 The clinical application of radioelectrocardiography Can Med Assoc J 70 574
7 BARR N L 1954 The radio transmission of physiological information Military Surgeon 114 79

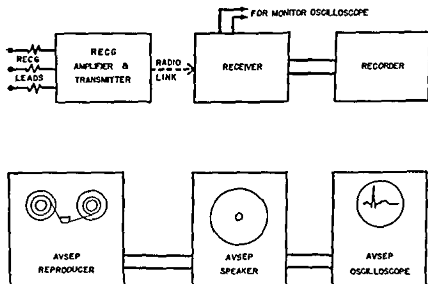


FIGURE 8 Simplified block diagram showing the flow sheet for radioelectrocardiography from the heartbeat to the detection of aberrant RECGs

are possible FIGURE 4 suggests a study of the exact why of the pulse pattern shown In other words the possibilities for obtaining new information on normal cardiac behavior appear to justify this development

An aim that suggests itself for future work in clinical medicine is that of aiding the clinician in his handling of the cardiac rehabilitation problem How well does the clinician know the boundary lines in the no man s land' of the physical regimen prescribed to the rehabilitation patient? A little radioelectrocardiography during the transition from hospital to home from home to part time work and from part time work to full time activity would provide the physician with some objective evidence of the effect of his prescribed regimen on the patient s cardiographic activity Would it not be possible and advantageous for the future practicing physician to take 20 minutes to put the previous day s tape in the AVSEP equipment and find a minor flurry of nonconforming T waves from yesterday at 2 o clock and advise his patient that yesterday s 2 o clock fight with his wife should not be repeated?

I shall close by suggesting the possible construction of a multichannel RECG to provide a stream of vector radioelectrocardiograms further to confound the data interpreters

Summary

Radioelectrocardiography and its instrumentation have been described It is offered as a basis for possible new contributions to cardiac physiology diagnosis and prognosis *pathology and therapeutics in the hands of appropriate* investigators in the biological sciences

I am indebted to Hans Hecht Paul D White and John Gilson for discussions and encouragement in this project

a constant desired temperature and humidity In this environment the T waves became sufficiently stable for experimentation after 30 to 60 minutes Holes in the glass cover were fitted with rubber cuffs allowing entry of the operator s forearms for free manipulation of the animal s heart and at the same time preventing an air exchange between outside and inside

In order to compare the results obtained in the incubator with those obtained from the intact dog cavity leads and subcutaneous leads from the overlying chest wall were taken in 9 closed chest dogs

The time course of repolarization was investigated by taking simultaneous leads from the epicardial surface and the underlying subendocardium in different locations of both ventricles In addition simultaneous surface leads were taken from corresponding points on both ventricles and from the apex and base of each ventricle The apex of the T wave was used as a reference point for timing because it appears to be the most accurate point for this purpose This was suggested previously by Lepeschkin[18]

In order to study *the influence of thermal changes on the repolarization process* hot and cold saline were applied to the epicardial and endocardial surfaces of the heart Because heat and cold caused very inconsistent changes of the T wave in preliminary experiments the following experiments were done with graded amounts of saline at comparable temperatures The amounts applied to the surface ranged from ¼ cc to 20 cc Simultaneous tracings were taken from the site of thermal change and from a point on the opposite side of the ventricular wall and in some cases from the opposite ventricle as well in order to determine distant effects Thermal changes of the endocardial layers were induced by injecting warm and cold saline into the cavity by means of catheters The warm saline was never above 46 C and the cold saline was never below 15° C In one dog ¼ cc of cold saline was injected intramurally and simultaneous leads were taken from the site of injection and from the corresponding epicardial and endocardial surfaces

In additional experiments designed to study the extension of thermal effects on repolarization 3 surface electrodes were placed on the left ventricular surface 1 to 2 mm apart One electrode served as a control 1 electrode was heated and 1 was cooled Tracings were taken simultaneously before and after inducing the thermal changes

A detailed report of these studies will be published elsewhere

Results

(1) *The polarity of the T wave* In surface explorations on the hearts of 16 dogs 122 leads were taken from the left ventricle and 163 from the right ventricle *A minimum of 18 leads was taken from each ventricle* at specific locations over the anterior and posterior surfaces Records with ST shifts were discarded The T wave was positive in 45 3 per cent of the records from the left ventricle and in 76 5 per cent of the records from the right ventricle T negativity was encountered in 40 8 per cent on the left chamber and in 11 7 per cent on the right The remainder were biphasic

T negativity was found more frequently over the base than at any other

STUDIES ON THE NATURE OF THE REPOLARIZATION PROCESS*

By Hubert Pipberger Lois Schwartz Rashid A Massumi
and Myron Prinzmetal

*The Institute for Medical Research Cedars of Lebanon Hospital Los Angeles Calif
and the Department of Medicine University of California School of Medicine
Los Angeles Calif*

The process of repolarization of the ventricular musculature represented by the T wave in the electrocardiogram has been studied relatively little as compared to that of depolarization This is due mainly to the fact that the T wave is very unstable in the usual experimental preparation

Literature

The presence of concordant polarity of the R and T waves in the usual electrocardiographic records has led to the concept of the ventricular gradient introduced by Wilson *et al*[1] and developed by Ashman and his associates[2 5] Some investigators concluded that the directions of depolarization and repolarization must be different and that therefore different parts of the ventricular musculature differed in their duration of activation The direction of repolarization was derived from concepts of the muscle strip preparation and was thought to proceed from epicardium to endocardium

The direction of repolarization however was not explained in such simplified fashion by the originators of the ventricular gradient concept Different theories were presented to account for the reversal of the repolarization direction Pressure and temperature differences across the ventricular wall were discussed as possible contributing factors in the genesis of the ventricular gradient[6 13]

Experimental work indicating an epicardial endocardial direction of the repolarization process has been reported by Hellerstein and Liebow[7] Their conclusions were based on studies of the T polarity The exact time course of repolarization however has never been clearly demonstrated

Material and Methods

Forty nine mongrel dogs were used in this study Details of the operative procedure anesthesia and respirator have been reported previously[14] Epicardial intramural and cavity leads were taken with minute silver wire unipolar plunge electrodes[15] The Sanborn twin beam electrocardiograph used for recording has a flat frequency response from 1 to 100 c /sec

The main obstacle to all studies on the T wave in the open chest dog is the continuous change of polarity and configuration of this deflection when the heart is exposed to room temperature Neither continuous warm saline sprays nor constant warm saline drips on the heart eliminated this difficulty entirely Finally the dogs were placed in an infant size incubator modified to maintain

Aided by grants from the National Institutes of Health Public Health Service Department of Health Education and Welfare Bethesda Md and the L D Beaumont Trust Fund Cleveland Ohio

found to be extremely large and no relationship between T polarity and the time difference was demonstrable

(4) *Influence of thermal changes on the repolari ation process* Application of cold saline resulted in an increased negativity of the T wave at the site of application Warm saline increased the positivity The QT interval was in most experiments shortened by heating and prolonged by cooling

As increasing amounts of cold or warm saline from ¼ cc to 20 cc were applied intermittently to the ventricular surface the polarity changes of the T wave recorded at the involved site increased concomitantly Simultaneous leads from the opposite side of the ventricular wall showed little or no T wave change when a small area was heated or cooled Reciprocal T wave changes appeared however when the area subjected to thermal change was increased by using greater amounts of saline In the latter case similar reciprocal T wave changes were observed even in leads from the opposite side of the heart

T polarity changes corresponding to those just described occurred when cold or warm saline was injected into the left or right ventricular cavity Due to the mixing of blood with the injected fluid no quantitative experiments could be performed by this procedure Reciprocal polarity changes were observed on the epicardial surface in most instances

In one animal ¼ cc of cold saline injected intramurally caused an increase in T negativity at the site of injection but no discernible changes in an epicardial and a subendocardial lead a few millimeters away

When 3 tiny surface electrodes were placed 1 to 2 mm apart on the left ventricle and one electrode was heated and another was cooled T wave changes inversion with cold and increased amplitude with heat were observed from the electrodes subjected to thermal changes but not from the third which served as a control

Warm and cold saline were applied to the surface of the human heart in one case and the results were similar to those in dogs

Discussion

(1) *The polarity of the T wave* The existence of a reciprocal relationship between T waves from opposite sides of the ventricular wall reported by Hellerstein and Liebow[7] could not be confirmed by our experiments Concordant positive polarity was found in a significant number of our experiments This was true not only of experiments in the incubator which closely approached a physiological situation but also of the records taken from animals with intact chests

It has been assumed by many workers that any segment of the intact heart running in an endocardial epicardial direction could be identified electrically as an isolated muscle strip Leads taken from each end of this *strip* were thought to record the electrical processes taking place in between A dipole front was supposed to proceed from epicardium to endocardium during repolarization giving rise to a positive T wave on the surface and a negative T wave in the cavity The presence of concordant positive T polarity in a large number of our experiments cannot be reconciled easily with this concept

surface location However, areas with negative T waves were distributed quite irregularly sometimes being very small and surrounded by areas of T positivity No regular pattern of distribution could be established as there was much variation from one animal to another

In 98 instances simultaneous leads were recorded from the ventricular surface and the underlying subendocardium on both ventricles T positivity was found on both sides of the ventricular wall in 47 3 per cent of the records from the left ventricle and in 70 7 per cent from the right The T was positive in the subendocardium and negative on the surface in 43 8 per cent from the left ventricle and in 17 9 per cent from the right Other combinations were found in the remainder

In the 9 closed chest dogs in which simultaneous leads were taken from the cavity and the overlying subcutaneous tissue the T waves were positive in all instances The left ventricle was investigated in 6 of these dogs the right in 3

(2) *Time course of repolarization* In 69 experiments on 11 dogs simultaneous leads were taken from the ventricular surface and the underlying subendocardium at specific locations in the base middle and apex of both ventricles The time course of repolarization was studied by measuring the time of occurrence of the apex of the T wave from the surface and comparing it with that from the subendocardium It was found that the subendocardial T apex preceded the surface T apex in 59 experiments The reverse occurred in 4 instances and in 6 cases the T apices were recorded simultaneously The mean time difference was 0 006 sec with the subendocardium preceding the surface The standard deviation was 0 005 sec with a standard error of 0 001 sec and a P value of less than 0 001 The mean time difference on the left ventricle alone was 0 007 sec whereas it was 0 005 sec on the right ventricle alone No statistically significant difference was found when the measurements from the left ventricle were compared with those from the right or when different zones of each chamber were compared the time difference *being approximately the same in all parts of the heart*

In 30 experiments time measurements of the T apices in simultaneous leads from corresponding points on the left and right ventricular surface showed that the right ventricle preceded the left by a mean time difference of 0 005 sec Since the standard deviation was 0 11 sec with a standard error of 0 002 sec and P of 0 02 to 0 05 the time difference was statistically significant with figures showing a relatively large range of distribution

Similar time comparisons were made between the T apices in surface leads from the apex and base of each ventricle in 20 experiments The mean time difference on the left ventricle was 0 003 sec the apex preceding the base On the right ventricle the mean difference was found to be 0 0006 sec the base being earlier than the apex The time differences here were calculated to have no statistical significance

(3) *Correlation of T wave polarity and the repolarization time course* The time difference between the subendocardial and epicardial T apices was plotted against the difference in magnitude of the same T waves The scatter was

found to be extremely large and no relationship between T polarity and the time difference was demonstrable

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Although negative T waves were observed more frequently over the basal region the most striking finding was a complete lack of uniformity in the T polarity distribution from one animal to another As in any electrical system including that of the heart the positive and negative charges must be equal Demarcation of positive and negative zones however was not demonstrable in the above experiments using unipolar leads in the arrangement described Our findings indicate that summated electrical fields rather than potentials from isolated muscle segments become demonstrable as long as the heart is in action as a whole These fields however, seem to be very irregular and cannot be defined in the same fashion as on the body surface This may be due to the complicating factors that arise in the near field of the heart about which very little is known A differentiation between summated electrical events from the heart as a whole and electrical effects from the site of leading has proved extremely difficult

(2) *The time course of repolarization* Besides the technical advantage of using the T apex as a time reference it was found that this part of the T wave showed different time relations in different parts of the heart This we attributed to local events an assumption however that is not yet proved

On the basis of T apex measurements we found a statistically significant time delay of the epicardium as compared to the subendocardium indicating that in most instances repolarization takes place earlier in the subendocardial layers than in the subepicardial layers From the distribution curve of our findings the reverse can be expected in 13 5 per cent of the total This seems to be a rather limited difference between the time course of depolarization and repolarization

The most striking finding was that the time course of repolarization cannot be related to the T polarity in our experiments This however seems to be due to the irregular polarity distribution encountered in the near field of the heart where many undefined factors may be active Neither a pointlike dipole equivalent concept nor the isolated muscle segment concept seem to explain this situation

The time correlation of the T apices from the right and left ventricular surfaces revealed a statistically significant delay of the left ventricle that may be due to the lesser thickness of the right ventricular wall repolarization being terminated earlier on the right ventricle

A comparison between the time of occurrence of the T apices from the apex and the base of each ventricle did not show a statistically significant time difference This may be due partly to the small number of experiments in this study A simultaneous repolarization of apical and basal regions of the ventricles would account however in part for a difference between the time course of depolarization and repolarization giving rise to the normal ventricular gradient As pointed out by Wilson and his associates[1] a number of local differences may exist and only the net electrical sum of differences is expressed in the ventricular gradient

(3) *The influence of thermal changes on the repolarization process* Since the first experiments of Bayliss and Starling[17] in 1892 many investigators have shown that the polarity of the T wave can be altered by thermal influences

Conclusions about the time course of repolarization have been drawn from those experiments Since we could demonstrate that polarity and time course may vary independently in such experiments as we have described these conclusions may be open to question

The increase in T negativity with a concomitant QT prolongation after application of cold can be explained by a local retardation of repolarization Opposite T and QT changes associated with the application of heat seem to be the consequence of a local acceleration of electrical recovery

It was shown that the magnitude of the polarity change of the T wave varies directly with the size of the area heated or cooled The smaller reciprocal polarity changes on the opposite side of the ventricular wall and in more remote parts of the heart also showed a direct relationship to the size of the area heated or cooled If we consider only the polarity change as such an increase in positivity or negativity must be balanced by equal charges in other regions The regions of positivity and negativity must be separated by an artificially induced dipole layer as a consequence of the thermal change Since the polarity changes on the opposite side of the wall are only a fraction of those encountered at the site of thermal change it can be safely assumed that the dipole layer set up by the thermal change is located close to the area heated or cooled This follows the laws of Helmholtz according to which the magnitude and the distance from the source of change are inversely related The polarity changes that were found after application of heat or of cold can all be explained on the basis of these laws A change restricted to a small surface area causes only minor changes at a distance of as little as a few millimeters Such small changes may not be perceptible with the equipment ordinarily used

The experiments in which cold saline was injected midmurally and in which tiny surface electrodes were heated and cooled further demonstrated that T wave changes due to small thermal effects may be restricted to minute zones without affecting leads a few millimeters away

The thermal T wave changes encountered in the dog seem to be analogous to those in the human heart that resulted from the application of warm and cold saline to the heart surface in one human case

Summary and Conclusions

(1) In 49 dogs myocardial repolarization was studied with unipolar electrodes at surface intramural and cavity levels The animals were placed in an incubator maintained at constant temperature and humidity to approximate a physiological environment

(2) *T wave polarity* was examined by simultaneous leads from the ventricular surface and the underlying subendocardium In 57 records from the left ventricle both surface and subendocardial T waves were positive in 47 3 per cent of the cases In 41 records from the right ventricle both T waves were positive in 70 7 per cent In 9 closed chest dogs simultaneous intracavity and overlying subcutaneous chest leads were taken and T waves were positive from all leads in all cases Thus under physiological conditions T wave polarity on opposite sides of the ventricular wall is not necessarily reciprocal

(3) *The direction of repolarization* in the ventricular wall was investigated

by timing of the T wave, using the T apex as the reference point. The subendocardial T preceded the simultaneously recorded surface T with a statistically significant mean time difference. The right ventricular surface T preceded the simultaneously recorded left ventricular surface T by a significant time difference. There was no significant difference between the apical and basal surface T waves, which may partially explain the difference in time course between depolarization and repolarization.

The time differences between the surface and subendocardial T waves showed no correlation with the polarity of these waves. The lack of correlation between the time course of repolarization and the T polarity may be due to the intricate situation encountered in the "near field" of the heart.

(4) *Thermal T wave changes.* Heating or cooling small areas of the ventricular surface caused local T changes but little or no changes in adjacent or distant leads. An increase in the area subjected to thermal change increased the local T alterations and also caused noticeable reciprocal changes in distant regions. These reciprocal changes, however, were considerably smaller in magnitude than those at the site of the thermal change.

All changes found could be reconciled with the laws governing the flow of current in volume conductors and those of potential distribution in electrical systems.

References

1. Wilson, F. N., A. G. Macleod, P. S. Barker & F. D. Johnston. 1934. The determination and significance of the areas of the ventricular deflections of the electrocardiogram. Am. Heart J. 10: 46.
2. Ashman, R. & E. Byer. 1943. The normal human ventricular gradient. I. Factors which affect its direction and its relation to the mean QRS axis. Am. Heart J. 25: 16.
3. Ashman, R. & E. Byer. 1943. The normal ventricular gradient. II. Factors which affect its manifest area of the QRS complex. Am. Heart J. 25: 36.
4. Ashman, R., M. Gardberg & E. Byer. 1943. The normal ventricular gradient. III. The relation between the anatomical and electrical axes. Am. Heart J. 26: 473.
5. Ashman, R. 1943. The normal human ventricular gradient. IV. The relationship between the magnitudes AQRS and G and deviations of the RS-T segment. Am. Heart J. 26: 495.
6. Grant, R. P. & E. H. Estes. 195[illegible]. Spatial Vector Electrocardiography. Blakiston. Philadelphia, Pa. & Toronto, Canada.
7. Hellerstein, H. K. & I. M. Liebow. 1950. Factors influencing the T wave of the electrocardiogram. An experimental study employing intracavitary and extraventricular (epicardial) leads. I. Effect of heating and cooling the endocardium and the epicardium. Am. Heart J. 39: 35.
8. Pipberger, H., K. Kaelin & P. H. Rossier. 1955. Vektorkardiographische Untersuchungen an Hypertonikern bei massiven Blutdrucksenkungen durch Hexamethonium. Ein Beitrag zur Theorie des Ventrikelgradienten. Cardiologia 27: 166.
9. Nims, L. F., B. Kartin, H. M. Chernoff & L. H. Nahum. 1948. Heart temperature and its relation to the T wave. Federation Proc. 7: 86.
10. Akman, L. C., F. N. Silber, A. J. Miller & L. N. Katz. 1949. Repolarization in the dog ventricle: effects of heating and cooling entire epicardial surface. Am. J. Physiol. 159: 492.
11. Chernoff, H. M. & L. H. Nahum. 1949. Order of recovery from excitation in dog, monkey and human heart: nature of ST segment and T wave. Federation Proc. 8: 24.
12. Lepeschkin, E. 1951. Role of temperature gradients within ventricular muscle in genesis of normal T wave of electrocardiogram and ventricular gradient responsible for it. Federation Proc. 10: 81.
13. Lepeschkin, E. 1951. Modern Electrocardiography. 1. Williams & Wilkins. Baltimore, Md.

14 Prinzmetal M E Corday I Brill R Oblath & H Kruger Assoc authors J Fields W Flieg A Goldman H Karpman S R Kennamer J A. Osborne A L Sellers & L A Smith 1952 The Auricular Arrhythmias Charles C Thomas Springfield Ill
15 Rothman S E Gerlach M Prinzmetal L Rakita & J L Borduas 1954 Studies on the mechanism of ventricular activity XIII Genesis of the depolarization complex in the mammalian heart Am J Physiol 179 557–569
16 Lepeschkin E & B Surawicz 1953 The duration of the Q-U interval and its components in electrocardiograms of normal persons Am Heart J 46 9
17 Bayliss W M & E H Starling 1892 On the electromotive phenomena of the mammalian heart Monthly Internat J Anat Physiol 9 256

THE REPOLARIZATION PROCESS OF CARDIAC MUSCULATURE
PANEL DISCUSSION

H H Hecht (*Moderator*) R H Bayley C Brooks P F Cranefield E Lepeschkin
H Schaefer D Sodi Pallares and E E Suckling

C BROOKS (*State University of New York Brooklyn N Y*) This monograph illustrates one of the principal modes of procedure of physiology The physiologist looks in two directions (1) he focuses his attention on minutiae attempting to make an ultimate analysis and he studies the membrane the origin of potentials and the basis for current generation (2) he also endeavors to view the entire situation trying to think in terms of the total organ the complete individual and the influencing factors and consequences of the total current spread

The group to which I happen to belong looks at less and less and we tend to think of cardiac performance in the light of the performance of the heart s component cells This is a somewhat new approach made possible by the recently developed methods of recording individual cellular or fiber activity There has arisen a host of new problems some of which have already been mentioned but I should like to review some of them to illustrate this new view

Weidmann has demonstrated that all cardiac cells are not identical in functional properties Some repolarize very rapidly while others possess a long plateau phase Hecht s illustrations show that there are at least three phases or three speeds of repolarization involved in the recovery process of cells after excitation Thus the total picture of the potential change recorded from the heart is a composite of deflections made up from the in phase and the out of phase performances of cells One can make substantial future progress with the interpretation of records based on assorted individual performances of cells cancellations and summations which emphasize or minimize the normally expected deflections It is possible to judge the extent to which certain abnormalities should modify the normal picture

To be more specific about some of these factors of great interest I should like to point out that there are numerous ways in which the response and the recovery processes that give the recorded potentials can be studied By recording potential changes one can see how the heart or its individual cells depolarize and then repolarize When other techniques are used to test the state of the heart and to analyze recovery more information is obtained and it can be seen that repolarization processes are not as smoothly progressive as the electrical recording techniques might suggest Stimulus testing (the application of current flow or stimuli) at various intervals in the cycle shows that during the terminal phases repolarization processes are not simple In the relative refractory period there is a phase of relative supernormality During the last few months it has been found in our laboratory that late in the cycle a stimulus of suprathreshold strength will produce an extrasystole When this stimulus is introduced progressively earlier in the cycle a point is reached at which it becomes ineffective but if introduced still earlier it becomes effective

again during a brief phase of the cycle even in an individual cell To be specific in the repolarization phase there is an interval of greater sensitivity to current flow anodal current flow

This dip phase or period of relative hypersensitivity to anodal current, might be merely a period when the membrane can be more readily repolarized —the cell repolarizes and then is excited by the anodal-off effect But why should anodal current repolarize heart tissue more readily during this interval than it does earlier and later in the cycle?

The conclusion suggests the use of still another technique that is the technique of impedance measurement Quick moment to-moment measurement of impedance changes and/or ion fluxes can be helpful in the search for knowledge of the dip phase the important interval of relative supernormality in the refractory period during which the heart if hit by a somewhat supernormal stimulus is vulnerable to fibrillation

The fact that a stimulus must be suprathreshold in order to stimulate and touch off fibrillation during this vulnerable period is not an absolute protection The ordinary action potential indicative of the spreading excitation that normally activates the heart is several times stronger than necessary for the excitation of normal tissue there is a considerable factor of safety Now if we turn to a consideration of injury potential and the instability of local areas caused by factors such as abnormal blood supply we perceive that a normally propagated wave of activation might touch off fibrillation by exciting this abnormal or unstable tissue during the vulnerable period

This is an incomplete treatment of complex matters but it does bring support to the contention that the entire heart and the function of its several parts should be studied in parallel and with multiple techniques Each new approach and new use of methods make new contributions possible for future investigations in the field

D Sodi Pallares (*The National Heart Institute Mexico D F Mexico*) I should like to return to the specific problem of the analysis of recovery processes by surface leads The question arises whether in spite of the precautions taken by Prinzmetal the results that he has reported apply to the interpretation of the human cardiac recovery process I shall confine my remarks to the direction of the T wave as we have encountered it in the normal heart In about twenty normal subjects we have recorded directly left and right sided intracavity potentials in all instances we have obtained negative T waves within both ventricular cavities I should add that due precaution was taken to avoid injury and consequent distortion of the patterns Because we have found negative T waves over the entire right thorax and positive T waves over the left anterior thorax we believe that the right epicardial surface yields only negative T waves and that the lateral surface of the free left ventricular wall yields only positive T waves Exploration of the posterior surface of the heart by bronchial leads again reveals negative T waves The only possible site for a vector to fulfill the above specifications would be one located within the free left ventricular wall This analysis leads us to assume that the activity of the septum is of little influence during the normal recovery process By way of confirmation vectorcardiographic studies show the T wave going to

the left, forward and downward If we produce left bundle branch block the left intracavitary T wave becomes more negative, while positive T s are recorded both within the right cavity and over the right epicardium The new position of the T vector would now be within the septum Placing this new T vector alongside the one drawn for the new excitation process makes their opposition immediately noticeable In the horizontal plane in the vectorcardiogram this is nicely brought out for therein the QRS loop is directed backward while the T loop is in an opposite direction Wilson insisted many years ago that the activation process determined to some degree the recovery process, this he termed the secondary factor Another important factor or factors however as Prinzmetal s experiments show is brought into play by such processes as heating and cooling the epicardial or the endocardial surface T wave changes of this sort are referred to as primary

H H HECHT (*University of Utah Salt Lake City Utah*) In the work described in the paper to which Sodi Pallares refers the apex of the T wave was used in much the same way that the peak of R has been used in so called unipolar leads to estimate the spread of excitation in direct leads One wonders if this is permissible even if one assumes for argument s sake that spontaneous recovery is a truly propagated response

R H BAYLEY (*University of Oklahoma School of Medicine Oklahoma City Okla*) I should like to point out that the duration of polarization occupies a long period of time It seems very reasonable that the majority of the units of the heart muscle must undergo repolarization during the same period of time and that in my opinion it would be very difficult for example to tell any direction from such recorded summation effects particularly from the shape or detection of any particular deflection such as the peak of the T wave during the recovery period I should like to hear more however about the propagated response of a recovery process

P F CRANEFIELD (*State University of New York Brooklyn N Y*) Interest in propagated repolarization was aroused by Weidmann s discovery that an all-or nothing repolarization can be induced in Purkinje fibers by the application of an anodal current that this repolarization has a discrete threshold and that it is propagated It subsequently came to my attention that Biedermann[1] had described a presumably similar phenomenon propagated relaxation in frog and snail hearts Biedermann observed and I have been able to confirm the fact that closure of a direct current through two electrodes on a frog or a turtle heart causes a visible relaxation under the anode if the closure occurs in late systole If the current remains closed relaxation occurs at the anode near the end of each successive systole Moreover upon the breaking of the current relaxation occurs at the cathode This relaxation thus follows an inverse Pflüger's law in that the anodal closing threshold is lower than the cathodal opening threshold The relaxation has the appearance of being propagated since it begins as a tiny bulge in the wall of the ventricle and the bulge rapidly enlarges in all directions The bulge naturally disappears as the whole ventricle passes into diastole Later workers challenged Biedermann by asserting that any relaxed area would bulge out in this manner beginning in the center and spreading toward the edges and therefore no propagation need be assumed

There is little question however that a clear cut propagation of relaxation even across small tissue bridges may be invoked in the snail heart

In my own investigation I have shown by motion pictures and by electrical recording that Biedermann s description of the radial spread of relaxation from the anode is correct and that repolarization, as indicated by shortening of the monophasic action potential occurs earliest nearest the anode Repolarization is accelerated to a progressively lesser degree at sites progressively farther from the anode These observations coupled with those of Weidmann might be taken as a demonstration of the existence of both propagated repolarization and relaxation in the intact heart There is unfortunately a subtle difficulty involved in the interpretation of the results repolarization is a spontaneously occurring process in which each cell is potentially its own pacemaker The speed with which the spontaneous process proceeds may well be increased by anodal current and that increase would be greatest at the anode thus giving an appearance of propagation Seldom if ever does the relaxation initiated at the anode appear to spread over the entire heart On the contrary the visible bulge apparently disappears as a result of the ordinary relaxation of the rest of the myocardium Occasionally the relaxation does seem to spread radially over the entire heart that is the tissue under the anode becomes a pacemaker for repolarization This observation provides by far the strongest argument for believing in the reality of propagated repolarization with con comitant propagated relaxation as a genuine phenomenon of the whole heart The reason that it is not always possible for the anode to set up a pacemaker for repolarization is that repolarization propagates very slowly which as Weid mann has pointed out would be a necessary consequence of the ionic movements on which it depends

The fact that propagated repolarization and relaxation can be induced by suitable stimuli is of considerable electrophysiological interest but it does not shed any light on the far more difficult question of whether propagation of re polarization plays any role in the normal electrical recovery of the heart It may at least be pointed out that a repolarized portion of the heart acts as an anode with respect to a depolarized portion and that therefore the possibility of propagation must exist On the other hand since the propagation of re polarization observed experimentally is so slow there would be no reason to expect a wave of repolarization to sweep over the whole heart beginning at the earliest repolarized spot Other areas would have repolarized spontaneously before any such wave could reach them It nevertheless seems probable that the anodal effect of recovered tissue in recruiting recovery in adjacent tissue is very important in explaining the spread of repolarization and therefore the shape of the T wave Certain areas may repolarize synchronously not only because they are depolarized synchronously but because of propagation of repolarization At the present time I would be willing to offer as a plausible working theory the idea that repolarization in the intact heart is a propagated phenomenon with multiple foci of origin

H Schaefer (*University of Heidelberg Heidelberg Germany*) As I see it the question lies in the extent to which the spontaneous repolarization process may be called a propagated event Propagation velocity is a term mean

ingful only in the case of a constant local time function of a propagating disturbance If we observe local disturbances such as monophasic action potentials of different shapes at different points of a fiber surface it is quite arbitrary whether we call this difference a deviation from the constant propagation velocity or an inhomogeneity of the local repolarization As the action potential is recorded in a single fiber however differences in propagation velocity' would imply that the monophasic action potential is composed of several individual units each displaying a different velocity Such a behavior could in turn be defined by Fourier analysis This concept, however is entirely hypothetical

E E SUCKLING (*State University of New York College of Medicine Brooklyn N Y*) I should like to return to the problem of the direction of the surface T wave with respect to QRS We find with the microneedle that the cell potential has a very large temperature coefficient If we lower the temperature of the single cell preparation slightly we greatly lengthen the action potential How does this relate to the electrocardiogram? We know that normally the inner myocardial layers begin to depolarize first The outside cells of the heart presumably start to do so a little later but they recover sooner When we cool the outside of the heart we may well lengthen the duration of the monophasic potentials of these cells and therefore we may obtain an inverted T wave in the surface electrocardiogram We see that we can get exact results applicable to surface electrocardiograms from an analysis of the single cell It is not necessary that this presumed difference be due to temperature but we can definitely modify monophasic membrane potentials by temperature

H H HECHT Suckling s remarks are of course an old story in a new dress I have pointed out that there are sharp differences in the temperature coefficients of various phases of repolarization What we do not know (and where we need more information) is whether the surface and the deeper layers actually show differences in the duration of recovery and whether they display different phases of repolarization which in turn could account for certain changes of the surface differential records that we have seen

E LEPESCHKIN (*University of Vermont College of Medicine Burlington Vt*) A problem that has been intriguing me ever since I became interested in electrocardiography is why is the T wave upright in leads that have an upright QRS in normal man and also in most normal animals? In other words why is there a ventricular gradient across the muscle wall? Under normal conditions all animals seem to have upright T waves on the epicardial surface Even dogs in whom the T waves may be inverted in almost any of the limb leads always have an area on the anterior surface of the thorax where the T wave is upright the variability of the T wave in limb leads in this animal can be attributed to the very loose mediastinum and the vertical position of the heart In 1939 I expressed at least a conjecture concerning the teleological reason for this, and now talking with Jane Robb I learned that she had also the same idea—that the internal muscle layers and the papillary muscles carry the tendons that hold the tricuspid and bicuspid valves and prevent them from opening into the atria These muscles must, therefore be the last to relax as long as there is

any pressure in the ventricle otherwise blood would regurgitate, and the work of the heart would be inefficient

The immediate cause of the late relaxation of the subendocardial muscle is another problem however I thought that hearts of all species have in common the attributes of possessing blood and also of beating and developing heat that must be dissipated in some way As the blood flows within the cavities of the heart and since it has a cooler temperature than the inside of the heart muscle the endocardial surfaces of the heart especially the trabecular regions that are completely surrounded by blood must have a longer duration of activity that is a later repolarization than the rest of the heart. According to my measurements with thermocouples in dogs[8] the average difference between the temperature inside the heart muscle and that of the intracardiac blood was about 1 to 2° F In a few experiments I tried to put a solution on the outside of the heart that had exactly the same temperature as the intraventricular blood that is I let it flow over the outside and the ventricular gradient which formerly had a positive value became zero This made it clear that a temperature gradient is at least one of the causes that determine the ventricular gradient of repolarization

H SCHAEFER The question is what does the gradient mean and can heat dissipation be regarded as the physical cause of the gradient? During the past several weeks we have measured carefully the influence of such temperature gradients We have tried to avoid any heat flux from the inside of the heart to the outside and we have seen that the ventricular gradient remained unchanged Furthermore the ventricular gradient has something to do with the excitation process because there is a strong positive correlation between the angles of the gradient and the angles of the QRS area in the frontal plane This means that all processes governing QRS must have a very decisive influence on the gradient This strengthens the consideration that Schmitt to my knowledge first pointed out and that goes against all modern concepts of the ventricular gradient my own included Schmitt assumed that the tapering of the fiber most probably has something to do with the ventricular gradient If this is true we easily understand why during propagation changes in the duration of the monophasic action potential might occur Since tapering occurs along the line of propagation it could be accompanied by changes in the form of the action potential

H H HECHT Perhaps we should now try to summarize some of the present concepts of cardiac repolarization the T wave and the ST segment If in ventricular muscle the order of excitation is altered the order of recovery must also be changed We need not belabor this point further What is of interest are the changes that occur during the spread of repolarization in the absence of any changes in the order of excitation These have been referred to as the primary T wave changes They may depend on the following two and somewhat interdependent factors

(1) The duration of the excitatory state may differ from one area to another so that complete intramuscular cancellation of the effects of excitation and of recovery will not occur This will result in a vectorial force pointing from the

area within which the systole is longer toward the area in which it is shorter This residual quantity of course, represents the effects of the ventricular gradient

(2) If there were a uniform change in the rate of recovery of all cardiac fibers a significant change would occur in the configuration of that portion of the surface record that is identified with the changed portion of the cellular recovery phase even if the ratio of the duration of excitation of one area compared to another (the ventricular gradient) has remained unaltered It is therefore at least theoretically possible to have primary changes of the T waves and the ST segment without alterations either in the magnitude or the direction of the ventricular gradient by changing the recovery process of each myocardial fiber simultaneously and in a uniform manner

One may express T wave changes in terms of cellular activity and in terms of the over all physiological characteristics of cardiac musculature Considering the former we know that the summit and falling limb of the T wave coincide with the last (third) phase of repolarization and that the major portion of the ST segment coincides with the characteristic plateau of the transmembrane potentials We also know that under reasonable physiological conditions phase differences and differences in duration of action potentials occur in adjacent fibers We know that changes in the slope of repolarization and changes in action potential duration can be induced easily by a variety of means This implies that local gradients may occur readily during the recovery phase and without assuming a propagated response of the repolarization process We are aware of the temperature sensitivity of the process or processes We do not know whether in general certain large areas within the ventricular myocardium show a shorter action potential duration than others whether for instance subepicardial muscle cells have a shorter duration than the cells lining the endocardial surface an assumption that is implicit in the usual explanation for the upright T wave of a normal surface electrocardiogram We do know however that the possibility for such a differential exists the difference in the duration of the ventricular myocardium the Purkinje fibers and the atrial musculature has been stressed What is more important perhaps is the fact that it can be shown that this difference is highly variable and can be made to change Beyond this a qualitative change in cellular recovery even if it is entirely uniform throughout the heart will alter the surface equivalent that in this respect behaves like the derivative of the action potential

Looking at this from the surface aspect we have stated that a ventricular gradient exists because certain areas presumably recover at a slower rate than others and that taking a cross section of myocardial musculature an upright T wave is recorded in a precordial lead for example if subepicardial layers recover faster than deeper sections (FIGURE 1) or if that section repolarizes in the opposite direction * Subepicardial lesions may cause a delay in repolarization of this area during which the gradient would disappear or reverse itself and a previously upright T wave would become inverted If the

* To simplify the discussion the influence of remote areas of the myocardium upon the magnitude and direction of such a direct lead has been assumed to be negligible which of course it is not

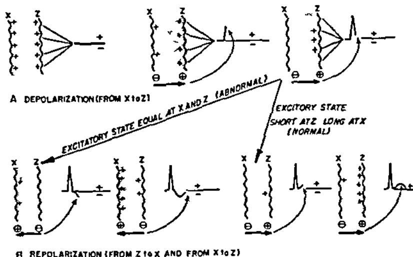


FIGURE 1 Current concepts of T wave changes A shows the depolarization of a ventricular muscle strip proceeding from X (endocardial) to Z (epicardial) In B if repolarization proceeds from X to Z also (equal duration of excitation in area X to area Z) an inverted T wave should be recorded and a recovery gradient would point from Z to X (left side of B) If Z recovers faster than X (right side of B) a recovery gradient points from Z to X and an upright T wave results A repolarized (resting) muscle segment is indicated by + Absence of this sign denotes that the area has depolarized or is not yet recovered

noxious influences persist the area finally fails to repolarize[3] and ST segment shifts occur In semischematic fashion this presumed course of events is illustrated in FIGURES 1 and 2 This concept assumes that under normal circumstances subendocardial layers although perhaps invaded earlier are slower to recover than epicardial segments There is as yet no proof of this assumption but there is good experimental support from the work of Macleod[4] Bayley *et al*[5] Hellerstein and Katz[6] and others The concept also has fitted well with interpretations of T wave changes and ST segment shifts that have been observed clinically and which agree with the experimental postulate that in direct unipolar epicardial surface leads inverted T waves and elevated ST segments indicate predominantly subepicardial upright T and depressed ST segments and subendocardial alterations[7, 8]

Weidmann s and Cranefield s observations on the propagated repolarization following anodal stimulation have injected a refreshing breath of air into the argument but for this theory it seems immaterial whether repolarization is or is not a propagated response and upright T waves recorded simultaneously from electrodes placed adjacent to epicardial and endocardial leads of the kind shown by Prinzmetal would merely imply that the two electrodes do not record from two opposing areas of repolarization Although the normal endocardial T wave was always inverted in many records of human endocardial electrocardiograms in our series concordance does occur under abnormal conditions

The real difficulty in a satisfactory explanation of T wave changes seems to lie in the fact that the observed facts obtained from single fiber records clearly

THE U WAVE AND AFTERPOTENTIALS IN CARDIAC MUSCLE: PANEL DISCUSSION

E. Lepeschkin (*Moderator*), L. N. Katz, H. Schaefer, A. M. Shanes, and S. Weidmann

E. LEPESCHKIN (*University of Vermont College of Medicine, Burlington, Vt.*): I should like first to make a few remarks about terminology. In the heart (FIGURE 1) the action potential shows a steep ascending phase (labeled zero by Weidmann[1]), a more or less steep descending phase or spike, a slowly descending plateau, and finally a more rapidly descending terminal phase. The latter phases were called 1, 2, and 3, respectively, by Fingl *et al.*[2] Phase 0 is attributed to the entry of sodium ions into the cell, phase 1 to the sudden stoppage of this entry, and phases 2 and 3 to a repolarization of the cell membrane due to the exit of potassium ions from the cell that is at first gradual and then more rapid. This action potential proper is followed by low-level potential changes that have been called the "afterpotentials" and designated as "phase 4" by Weidmann.[1] In distinguishing between the two we see that the afterpotential is much smaller in amplitude than the action potential proper and that in the heart and skeletal muscle relaxation begins with the end of the action potential proper. The U wave of the electrocardiogram, which corresponds in time to cardiac afterpotentials, appears after the second heart sound, that is, after ventricular relaxation has begun.[3,6] During the afterpotentials there may be changes in the diastolic myocardial tonus, but these are usually insignificant compared to the systolic contraction.[7,8] A third point of differentiation is the excitability of the heart. The action potential proper corresponds to the refractory period, which usually ends with the rapid descent of this potential or with the apex of the T wave, while the afterpotentials correspond to the small phasic changes of excitability that follow the refractory period. The negative afterpotential corresponds to the supernormal phase of excitability and the positive afterpotential corresponds to the subnormal phase and to the gradually increasing excitability during the diastolic period.[1,7,9] These relations are completely analogous to those in nerve, as we shall hear from Shanes.

The designations "positive and negative afterpotentials" are a little confusing to the cardiologist because the negative afterpotential is actually positive in the curve showing the potential variations of the inside of the cell, such as that obtained with the intracellular electrode. The reason it is called "negative" is that it indicates negativity of the extracellular space, which determines the configuration of any curve taken from the uninjured organ. In order to avoid confusion it may be preferable to use the term "hyperpolarization" for the positive and "incomplete polarization" for the negative afterpotential, using the degree of membrane polarization just preceding the action potential proper for comparison. We shall not employ the term afterpotential in reference to anything but the transmembrane potential. For instance, I am not in agreement with Sjostrand,[10] who designates as afterpotential what I consider to be a separate slow portion of the U wave in surface leads.

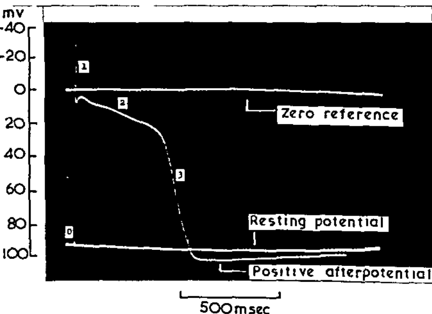


FIGURE 1 Intracellular action potential as it was normally recorded from excised Purkinje fibers of the sheep showing a positive afterpotential The phases 0 (ascent) 1 (descent of the spike) 2 (plateau) 3 (rapid repolarization) and 4 (afterpotential) are indicated on the curve

One of the reasons for my detailed study of the U wave and the afterpotentials was the fact that the U wave is one of the component parts of the electrocardiogram most constantly affected by potassium imbalance It was actually Shanes studies concerning the effect of potassium on the afterpotentials in nerve that started me in this direction I should like to ask Shanes to present a short summary of his concept

A M SHANES (*Laboratory of Pharmacology and Toxicology National Institute of Arthritis and Metabolic Diseases National Institutes of Health Public Health Service Department of Health Education and Welfare Bethesda Md*) I should like to outline briefly factors in afterpotential production that have come to my attention through studies on nerve

Afterpotentials may be regarded as any minor fluctuations in the potential difference across the cell membrane immediately following the large electrical transient known as the spike Thus in the squid giant axon the spike is promptly succeeded by a return of the membrane polarization to a level temporarily greater than when at rest This may be called the positive overshoot It should be distinguished from the later more prolonged hyperpolarization that can be accentuated by the drug yohimbine I prefer to restrict the term positive afterpotential to the second hyperpolarization Between the positive overshoot and the positive afterpotential there is frequently found a tem



FIGURE 2 *A* shows the action potential (upper record) from a squid giant axon with only the base of the spike and the succeeding positive overshoot and oscillations and the corresponding unbalances in a Wheatstone Bridge (lower record) showing the fluctuating increases in conductance as a result of the passage of this action potential between platinized transverse electrodes (20 msec sweep) *B* shows the same phenomena with a tenfold slower sweep demonstrating in addition the more prolonged negative afterpotential and the associated elevated conductance From Shanes *et al* [13]

porary depression of membrane potential to below the normal that can be enhanced by veratrum alkaloids such as cevadine and veratridine this is known as the negative afterpotential

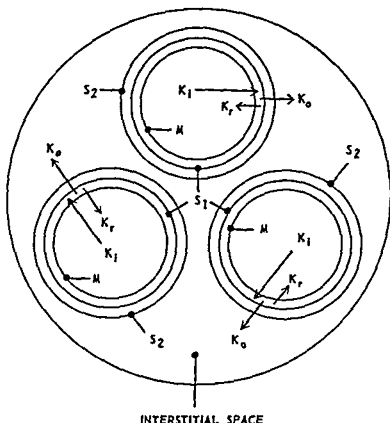
The upper half of FIGURE 2 shows the beginning and end of the spike the positive overshoot and the minor oscillations of potentials that are usually accentuated after treatment with the alkaloids of veratrum The lower half of the figure shows the corresponding changes in membrane conductance When the time scale was compressed we saw that this negative afterpotential the residual depolarized state of the fiber disappeared only very slowly and if this had been followed further especially in the presence of still another drug yohimbine we should have observed the positive afterpotential corresponding to the period of subnormality The transverse impedance technique developed by Cole was used in these studies The prolonged small increase in the conductance of the membrane which decays with the same time constant as the afterpotentials might be considered to be caused by an increase in permeability although this is not the only possible interpretation

At least two mechanisms may be postulated to account for afterpotentials One depends on fluctuations in the permeability of ions relative to each other

Thus it can be shown on the basis of equations such as those derived by Goldman[11] that an increase in potassium permeability relative to the permeability to sodium and chloride will increase the membrane polarization as appears to be the case for the positive overshoot whereas an increase in sodium and/or chloride permeability relative to potassium permeability will reduce the membrane potential The specific permeabilities involved may be elucidated by following the changes in electrical conductance associated with the afterpotentials and by comparing them with the fluctuations predictable from theory [11, 12]

A second mechanism partly a secondary consequence of permeability changes of the membrane results from the transitory rise or fall in the potassium concentration at the outer surface of the fiber [1, 17] A rise in this concentration will depolarize and increase the electrical conductance of the membrane while the converse will have the opposite effect Since the liberation of potassium during the spike is now well known one must determine (1) what governs the accumulation of potassium at the fiber surface (2) what governs its disappearance from the surface (3) how these concentration changes are related to afterpotential production and (4) how afterpotentials produced by potassium fluctuations may be distinguished from those resulting from changes in the relative permeabilities

FIGURE 3 indicates diagrammatically factors that would govern the accumulation and disappearance of potassium from the fiber surfaces in a hypothetical nerve of three fibers mounted in a moist chamber The size of the arrows indicates the quantity of potassium transferred Thus the amount of potassium liberated during the impulse is K the amount released over a given interval through sheaths S_1 and S (myelin and Schwann sheaths) is K and the amount reabsorbed in the same interval is K In the muscle fiber S_1 and S_2 could correspond to the sarcolemma and the connective tissue in the interstitial spaces respectively Presumably the potassium trapped between the membrane M and the innermost extracellular sheath S_1 tends to keep M depolarized Sheaths S_1 and S_2 are assumed to be electrically indifferent to potassium The amount of trapping depends on the speed with which the potassium is released compared to its rate of diffusion away and its rate of reabsorption while the subsidence of accumulated potassium depends only on diffusion and reabsorption A nerve without circulation and in a moist chamber as in FIGURE 3 does not permit removal of the potassium escaping to the interstitial space *Therefore with sufficiently rapid and continuous* stimulation outward diffusion through the sheaths finally will not occur because of the absence of a diffusion gradient so that potassium removal then results only from reabsorption during and following activity But if the nerve is immersed in a large volume of solution following activity the decline in extracellular potassium (and in potassium induced depolarization) will be faster owing to a decline in external potassium by diffusion out of the nerve as well as by reabsorption [14, 15] Indeed in the last case reabsorption will continue even after the potassium level between M and S_1 has returned to normal owing to the earlier extensive depletion of potassium from the fibers Because of the diffusion limitation imposed by S_1 and S the potassium concentration adjacent to M will therefore fall below the resting level thereby giving rise to a positive afterpotential [14, 16]



FIGURES 3 Schematic cross section through a nerve illustrating the diffusion spaces

The reabsorption of potassium may be regarded as the result of two processes operating in parallel (1) an electrochemical or passive one that is one governed solely by the differences in potassium concentration and electrical potential across the membrane and (2) a metabolic one that is one controlled by release of energy by the cell which in an unknown manner sucks in the potassium ion Evidence for a potassium pump is now good for giant invertebrate fibers[18] and for vertebrate fibers [19]

As shown in FIGURE 3 the amount of potassium K_o escaping through the sheaths exceeds the amount reabsorbed This may be the situation in a nerve for single impulses and it certainly is the case for rapid stimulation This means that reabsorption must continue to operate for an appreciable time after activity to restore the original potassium level In the heart which maintains a high intracellular potassium level during sustained beating reabsorption during the diastole and possibly, during the latter part of the systole (K)

must equal the potassium lost from the fibers during the systole including that picked up by the circulation

The effectiveness of the accumulated potassium in causing a depolarization depends on the selectivity of the membrane to potassium on the concentration attained and on the potassium concentration surrounding the fiber just prior to the potassium release The selectivity depends on the time course of recovery of the membrane from the permeability changes during the spike The concentration attained for a given potassium loss is governed by the effective volume of the space between the membrane and the surrounding extracellular sheaths The space in the squid axon has been estimated to be 300 Å[17] The potassium level just prior to release may play a part by determining the gradients of concentration and of the electrical potential that drive out the potassium However it may also act by virtue of the well known semilogarithmic relation between the membrane potential and the potassium concentration Thus a given potassium release may produce say a 1 mv change at the normal extracellular potassium level but if the extracellular concentration is doubled then twice the previous potassium release would be required for the same electrical change of 1 mv

In terms of our current picture of processes during and following activity in nerve the action of pharmacological agents and altered physical conditions on similar events in the heart may be as follows

(1) *To alter the amount of potassium liberated during the contraction* Veratrum alkaloids and low temperature increase the loss during the nerve impulse[16, 20] while stabilizing agents such as local anesthetics which reduce permeability to ions[19, 21, 22] may have the opposite effect Wilde s work described earlier on page 693 certainly demonstrates that potassium release occurs during systole

(2) *To change the rate of potassium diffusion through surrounding sheaths* (for example through the sarcolemma) Low temperature for example slows this rate The action of experimental agents on such sheaths must be considered a possibility until contrary evidence is available

(3) *To modify the rate of potassium reabsorption* If the passive return is a significant fraction of the total reabsorption then altered permeability or modified electrochemical gradients will affect the rate of potassium reabsorption Thus low temperature and stabilizing compounds which reduce permeability would slow it down and veratrum alkaloids which act oppositely would enhance it Active metabolic reabsorption would be directly dependent on the rate of metabolism In nerve we have found that the passive uptake under normal metabolic conditions is so small that cocaine which lowers permeability has only a minor effect at best on the total uptake[19] the cocaine effect becomes apparent when the metabolic contribution to transport is reduced

(4) *To alter the time course of permeability changes following activity* Veratrum alkaloids and low temperature appear to prolong the state of increased permeability in nerve

In conclusion I should like to call attention to the possibility that a considerable change could be produced in the extent of the fluctuations of potassium

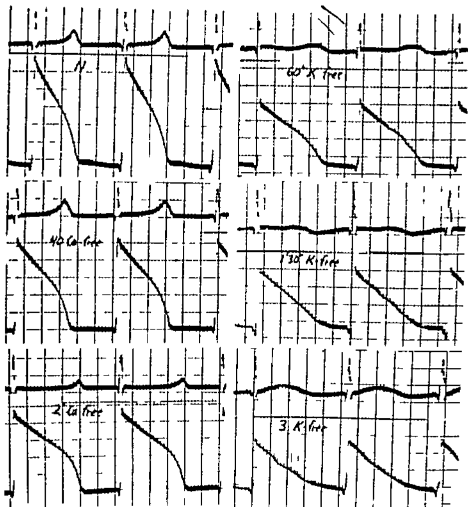


FIGURE 5 Electrocardiogram and the synchronous monophasic action potential (suction electrode) of a rabbit heart perfused with Krebs Henseleit solution showing the depression of the negative afterpotential following the withdrawal of calcium and the accentuation of the negative afterpotential and the U wave subsequent to the withdrawal of potassium [2]

tential proper and corresponding in time to U waves whenever they were present in the synchronously registered electrocardiograms (FIGURE 5)

The idea that U waves correspond to afterpotentials was first proposed by Nahum and Hoff in 1939[26] FIGURE 6 shows how the normal U wave might originate as the difference in the duration of negative afterpotentials just as the T wave can be interpreted as the difference in the duration of the action potential proper in different parts of the heart In this figure the solid line curve in the upper half is a copy of the intracellular action potential taken by Hecht from the surface fibers of the chicken heart [2] If we assume that the action potential of the subendocardial ventricular muscle layers begins earlier and lasts

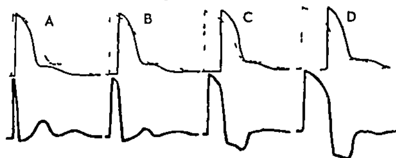


FIGURE 6 A shows the schematic construction of the normal electrocardiogram with upright T and U waves as a difference between two action potentials with negative afterpotentials. In *B* through *C* the time difference between these action potentials is progressively increased resulting in inverted T waves with low upright U waves and finally in inverted T and U waves. From Lepeschkin

considerably longer than that of the subepicardial layers (dotted curve of FIGURE 6 see discussion on the T wave in the preceding panel discussion) the difference between the two will yield the normal electrocardiogram with upright QRS and T. If the negative afterpotential begins with the end of the action potential proper and has an approximately equal duration in all parts of the heart, an upright T wave will normally be accompanied always by an upright U wave, and this is actually observed. Parts B through D of FIGURE 6 show what would be expected if the intraventricular conduction time were increased progressively as in bundle branch block or ventricular premature beats: as the QRS complex becomes wider, the T wave becomes inverted, and the U wave at first becomes smaller and then finally becomes negative. This is also confirmed by observation.[4]

While in general the polarity of the U wave follows that of the T wave, the U wave tends to show maximum positive potential in leads V3 (V2–V4) and may be positive in these leads even when T is negative (for instance in the juvenile T wave pattern or in primary localized T wave inversion).[4] In 1955 a book on the U wave was published in Italy by Furbetta, Santucci and Bufalari.[5] These investigators studied the U wave distribution in the exposed hearts of dogs. Under normal circumstances the U wave in dogs is very small but when the heart is cooled a definite U wave appears and the maximal positive voltage of these U waves on the surface of the exposed heart corresponds almost exactly to the part of the ventricles where the papillary muscles have their insertion. The authors attribute the U wave to a longer duration of the action potential in the papillary muscles, but I believe that this is incorrect because their own monophasic tracings from the papillary muscles show that the duration of the action potential proper is the same as in the rest of the heart. I think the best explanation for these discrepancies between the duration of T and U can be found in the work of Dudel and Trautwein[23] in Schaefer's laboratory, who found that the amplitude of the negative afterpotential can be increased from about 4 to 20 per cent of the action potential proper by stretching (FIGURE 4). The papillary muscles must bear the weight of the en



FIGURE 7 A shows very tall U waves in a patient with severe diarrhea and a serum potassium of 1.6 mEq per liter. B shows the normal U waves after the serum potassium has returned to the normal value of 4.1 mEq per liter.

tire ventricular pressure resting on the large A V valves and because of the resultant stretch the negative afterpotentials and the U waves should be of especially great amplitude in these regions.

TABLE 1 summarizes some of the factors that cause changes of the U wave and the effect of these factors on negative afterpotentials. One of the most important factors that increases the U wave is a low extracellular potassium concentration. Under this condition the U waves can become much taller than the T waves (FIGURE 7)[4, 7] and at the same time the negative afterpotentials increase (FIGURE 5).[25] On the other hand an increase in the extracellular potassium concentration decreases both the U waves and the negative afterpotentials.[7, 5] The explanation of these changes would be that with a low external potassium more potassium would leave the cell during phases 2 and 3 of the action potential while reabsorption of this potassium into the cell would be slower taking place against a higher gradient. At the same time as Shanes has pointed out the same amount of potassium would produce a greater depolarization. The slight depolarization of the cell membrane caused by the negative afterpotential should make it easier to depolarize the membrane to its critical potential when a spontaneous action potential takes place; in other words the afterpotential should correspond to a supernormal phase of excitability. A supernormal phase was actually seen by Segers[7] in all frog hearts that showed negative afterpotentials and this supernormal phase was abolished by potassium. Measurements of the cardiac excitability in humans have not yet been made but the fact that low serum potassium frequently leads to coupled extrasystoles[4] and that these are abolished by potassium would agree

TABLE 1

SOME OF THE FACTORS THAT INFLUENCE THE U WAVE AND THE EFFECT OF THESE FACTORS ON NEGATIVE AFTERPOTENTIALS AND MYOCARDIAL EXCITABILITY

	U wave	Negative afterpotentials	Supernormal phase of excitability	Coupled extrasystole
Long diastole	+	?	?	+
Stretching	+	+	+?	+
Cooling	+	+	+?	?
Low ext potassium	+	+	?	+
High ext potassium	−	−	?	−
Low calcium	−	−	?	−
High calcium	+	±	+	+
Epinephrine	+	+	?+	+
Acetylcholine	?	−	?−	−
Veratrine	±	+	+	+
Digitalis	+	+	?	+
Quinidine	+	+?	?	−

with the concept developed above The increase in the amplitude of the U wave [4] as well as that of the negative afterpotentials[7] caused by adrenalin may be related to an increased potassium outflow from the heart muscle or to the decrease in the serum potassium that follows administration of this drug Coupled extrasystoles are common after adrenalin but I do not know of any studies on the supernormal phase

We have heard that stretching increases the negative afterpotentials[23] and also the excitability of the heart [9, 28] In the light of what Shanes has said stretching could increase negative afterpotentials by increasing the density of the connective tissue fibers that surround the myocardial cell and impede the diffusion of the potassium liberated during the systole The increased amplitude of the U wave after long diastolic pauses[4] may be related to the greater diastolic filling of the ventricles but an important factor in this is that greater asynchronism of afterpotentials will develop during the longer systole Cooling increases the amplitude of the U waves[5] and the negative afterpotentials in nerve and it has also been found to increase the supernormal phase of excitability [9] Shanes mentioned that this could be caused by a slowed diffusion and reabsorption of the potassium that has left the cell during the action potential Veratrine increases the negative afterpotentials and the U waves and causes coupled extrasystoles [4] the mechanism in this case as Shanes mentioned could be an increased potassium loss during the action potential as well as slow potassium reabsorption High extracellular calcium has been found to increase negative afterpotentials in the frog [7] and U waves in humans [4] while low calcium has been shown to decrease the afterpotentials in frogs[7] and rabbits [25] as well as U waves in humans [4] This could possibly be caused by a decrease in the cell permeability and the potassium reabsorption after calcium On the other hand high calcium often leads to coupled extrasystoles

Digitalis increases the negative afterpotentials in the frog[7] and also increases the U wave in man this was evident in a study we just concluded with B

Surawicz in which we compared digitalized patients with nondigitalized patients having the same heart rate and QRS voltage On the other hand, coupled extrasystoles are one of the most constant signs of digitalis toxicity The increase in negative afterpotentials under the influence of digitalis could be explained by the inhibition of diastolic reabsorption of potassium that Szent Gyorgyi[30] and Hajdu[31] consider as one of the most important effects of digitalis The only factor that does not affect the negative afterpotentials the U waves and excitability in the same way is quinidine which increases the U wave in man[4] but decreases the excitability of the heart and causes coupled extrasystoles to disappear The explanation in that case could be that quinidine depresses the threshold to such an extent that even a slight supernormal phase which may be due to negative afterpotentials will not cause the appearance of premature beats

H SCHAEFER (*University of Heidelberg Heidelberg Germany*) The facts as far as I know them from Lepeschkin[4] are the following

(1) The U wave potential goes nearly in the same direction as the T wave and both are apparently linked very closely

(2) This means that the U vector in the frontal plane shows its positivity down and to the left

(3) At the time of the appearance of the U wave the membranes of heart fibers show only afterpotentials in the common sense that is potentials surviving the end of the so called monophasic action potential

(4) Nearly all drugs or other external influences act perfectly parallel on afterpotentials and on the U wave

(5) At the time of the appearance of the U wave the heart relaxes

(6) The higher the volume of the stroke in general the higher the U wave

(7) There are important exceptions the empty heart or the heart with a critically reduced stroke volume (in postural hypotension) also shows high U waves

(8) The influence of sudden distension on membrane potentials is practically absent

(9) The stretching of the muscle fiber leads to a strongly augmented negative afterpotential

(10) The development of U waves coincides under experimental conditions with the development of increased *negative* afterpotentials

Thus we have the facts The following critical remarks may be made against the common attempt of paralleling afterpotentials and U waves

(1) We never measured the change or development of U waves and after potentials at the same heart fiber of warm blooded animals

(2) The influence of drugs and hormones is biphasic in some cases and we are not always sure which phase we are observing

(3) The action of drugs and hormones may be indirect in some cases This means that some substances may act by their own power others by starting a secondary process For example insulin adrenalin and similar drugs may act partly or completely by influencing the peripheral vascular resistance and augmenting the stroke volume or one drug may act by influencing the K exchange rate or the K concentration inside or outside the fiber membrane

The following are purely logical considerations

(1) In my opinion big muscle masses must be involved in the production of a U wave and it is impossible to explain this only on the basis of some deviations of the papillary muscles

(2) Even if a strong negative afterpotential were present as a source of U wave potential the low afterpotential could scarcely exceed 10 per cent of the QRS area Moreover this amount must be strictly discordant if the long lasting afterpotential is the only source of the U wave Without having a nonhomogeneous time course of the repolarization of the various parts of the heart the ventricular gradient must obviously include the U wave and the U area cannot exceed an area caused by the repolarization forces of the afterpotentials Since the U area at least in some cases may exceed 10 per cent of the QRS and is of completely different direction namely concordant to QRS and T the U wave potentials must have their origin in the sense of potential source either in nonhomogeneous repolarization processes in various parts of the myocardium during the time of negative afterpotentials or in a completely different electrical event in the heart as for example in the stretch potentials

(3) In the case of stretch potentials an electric field of the U wave similar to that associated with the afterpotential hypothesis develops only if the various parts of the ventricle are stretched in a different velocity or intensity

(4) From the potential fields it is impossible to conclude whether the source of the U wave assuming the validity of an afterpotential hypothesis is a negative or a positive afterpotential If it is a negative one as indicated by the facts presented by Lepeschkin the basis of the heart or any inner layers compared with the apex or outer layers should develop the higher negative afterpotential

We may try to bring all these different points together into a hypothesis that will cover all the facts and fit all the logical points

The hypothesis strongly emphasized in my book on electrocardiography[3] that *stretch* potentials alone may give rise to the U wave does not seem to interpret the sum total of facts and problems known today It disagrees in detail with the correlations and the identity in the direction of the T and U waves and with the fact that no stretch potentials at all are registered in isolated muscle fibers The hypothesis that *afterpotentials* alone may give rise to the U wave disagrees with the fact that the strong potentials of the U wave are too strong to be the consequence only of the repolarization of a negative afterpotential In addition the polarity of the U wave is not explained by the afterpotential theory alone and the correlation between the direction of the T and the U wave is also not explained It is therefore obviously unsatisfactory to assume that either the afterpotential hypothesis or the stretch potential concept is the only possible explanation of the U wave

In conclusion

(1) The U wave must be considered under theoretical assumptions quite similar to those applying to the T wave It must be the result of a nonhomogeneous repolarization process occurring at the time of the afterpotentials If the parallel between the drug influence on the U wave and on the negative after

potentials holds true then the U wave must be a nonhomogeneously declining negative afterpotential

(2) To understand the U wave we must understand the law of this nonhomogeneity of repolarization The coupling between T and U shows that the U wave strongly depends on all the processes governing the ventricular gradient at least on the spread of excitation expressed in the orientation of fibers and the time sequence of their depolarization This coupling extends even to the correlation with the stroke volume as the augmentation of stroke volume leads to an increase of the U wave whereas the augmentation of the pulse pressure amplitude—including the stroke volume—leads to an augmentation of all the positive T areas and this applies to the ventricular gradient

(3) As long as we are lacking a correct and complete theory of the T wave and of the ventricular gradient we shall scarcely come to a sufficient interpretation of the U wave For the moment the best interpretation is that a *negative afterpotential is strongly influenced by mechanical (hemodynamic) factors* The stronger and swifter the heart fibers are stretched by the diastolic filling the more intense the negative afterpotential can be

The direction of the potential differences along the various parts of the heart is obviously controlled by the same process that governs the direction of the T wave This process is a nonhomogeneousness strongly correlated with the anatomical distribution pattern of all myocardial fibers Without adhering to any particular T wave or ventricular gradient theory the negative afterpotentials probably show differences in their repolarization slope which depend directly on the morphology of the heart

(4) This morphological coupling may be of the following character the T wave may be governed by nonhomogeneities caused by a condition such as the tapering of the fibers oriented from inward to outward and correlated directly with the spreading process going on more or less perpendicular to the ventricular surface The U wave may be governed by mechanical factors depending on this same perpendicular direction

(5) The stronger the stroke volume the more nonhomogeneous the negative afterpotentials Strong nonhomogeneous afterpotentials however may be produced easily in empty hearts since in these the difference in the mechanical factors inside and outside the ventricular wall may be higher than in hearts beating with normal stroke volumes The nonhomogeneousness may go through a minimum with the stroke volumes increasing from zero to comparatively high values

(6) A simple model will produce the necessary theoretical results If we consider the heart as a ball formed by concentric muscle layers the distention during the filling phase of the diastole may be calculated easily In any case the distention of the inner layer compared with the outer layer becomes greater the more the end systolic volume decreases (empty heart postural hypotension) and the more the stroke volume increases Both events lead to the same effect an augmentation of the ratio between the length of the muscle in the contracted and the distended state expressed in percentage of the total fiber length

If therefore the negative afterpotential is increased by stretch in a fairly

quantitative manner this geometry of stretch in the inner and outer layers of the ventricular wall would account for the U wave in a completely sufficient manner thus explaining (1) the correlation of the T and U waves (2) the orientation of both by their basic individual mechanism mechanical distention and fiber tapering or intramural pressures responding in a direction perpendicular to the ventricular wall (3) the polarity of the U wave which is negative in the inner layers (4) its correlation with negative afterpotentials and their mutual dependence on drugs (5) its dependence on the stroke volume (6) and its behavior in the empty beating heart

All these remarks are concerned exclusively with the U waves in normal hearts In abnormal hearts stronger afterpotentials of metabolic origin distributed in a nonhomogeneous manner are supposed to be the physical basis of long lasting U waves of various directions

E LEPESCHKIN I should like to ask Katz to correlate some of the clinical findings on the U wave with what we have heard tonight

L N KATZ (*The Cardiovascular Department Medical Research Institute Michael Reese Hospital Chicago Ill*) This discussion has been very stimulating but there are still some gaps in our knowledge I think we need to know a great deal more about the positive and negative afterpotentials in order to understand their effect upon the U wave We also need to know more about the occurrence of the U wave in surface leads and in the cavity leads of clinical cases

From my personal experience I know that occasionally in heart strain and in cases of recent or old myocardial infarction one may encounter isolated abnormalities of the U waves I also know that after treatment with digitalis and with quinidine there are U wave changes The quinidine contour of U and T is reminiscent of that seen with certain electrolyte disorders

From the clinical point of view the most important thing is the T U relationship in hyper and hypopotassemia There is an inverse relationship between the T and U heights in these cases the T wave becoming taller and tent shaped in hyperpotassemia and the U wave decreasing the reverse is true in regard to their amplitudes in hypopotassemia

I have enjoyed the discussion particularly that of Schaefer with whom I disagree only in that I cannot see the importance of the relationship of the U wave to stretch

The U wave is somewhat related to the ST T configuration This relationship to the ST T deflection is closer than that to the QRS complex which is a different way of expressing what Schaefer has said more eloquently We should talk about changes in the U wave that are secondary to QRS alterations and to S T and T alterations and we should differentiate them from those that are primary just as we do in the case of the T wave

I am intrigued with the idea that the U wave is caused by changes in after potentials especially the negative afterpotentials I agree with Schaefer that the U wave cannot originate in the specific tissues or papillary muscles because quantitatively potentials created in these fibers are small compared to the potentials of ordinary ventricular muscles which most likely are responsible for the U deflection I should say therefore that it is an inequality of potentials

potentials holds true then the U wave must be a nonhomogeneously declining negative afterpotential

(2) To understand the U wave we must understand the law of this nonhomogeneity of repolarization The coupling between T and U shows that the U wave strongly depends on all the processes governing the ventricular gradient at least on the spread of excitation expressed in the orientation of fibers and the time sequence of their depolarization This coupling extends even to the correlation with the stroke volume as the augmentation of stroke volume leads to an increase of the U wave whereas the augmentation of the pulse pressure amplitude—including the stroke volume—leads to an augmentation of all the positive T areas and this applies to the ventricular gradient

(3) As long as we are lacking a correct and complete theory of the T wave and of the ventricular gradient we shall scarcely come to a sufficient interpretation of the U wave For the moment the best interpretation is that a negative afterpotential is strongly influenced by mechanical (hemodynamic) factors The stronger and swifter the heart fibers are stretched by the diastolic filling the more intense the negative afterpotential can be

The direction of the potential differences along the various parts of the heart is obviously controlled by the same process that governs the direction of the T wave This process is a nonhomogeneousness strongly correlated with the anatomical distribution pattern of all myocardial fibers Without adhering to any particular T wave or ventricular gradient theory the negative afterpotentials probably show differences in their repolarization slope which depend directly on the morphology of the heart

(4) This morphological coupling may be of the following character the T wave may be governed by nonhomogeneities caused by a condition such as the tapering of the fibers oriented from inward to outward and correlated directly with the spreading process going on more or less perpendicular to the ventricular surface The U wave may be governed by mechanical factors depending on this same perpendicular direction

(5) The stronger the stroke volume the more nonhomogeneous the negative afterpotentials Strong nonhomogeneous afterpotentials however may be produced easily in empty hearts since in these the difference in the mechanical factors inside and outside the ventricular wall may be higher than in hearts beating with normal stroke volumes The nonhomogeneousness may go through a minimum with the stroke volumes increasing from zero to comparatively high values

(6) A simple model will produce the necessary theoretical results If we consider the heart as a ball formed by concentric muscle layers the distention during the *filling phase of the diastole may be calculated easily In any case* the distention of the inner layer compared with the outer layer becomes greater the more the end systolic volume decreases (empty heart postural hypotension) and the more the stroke volume increases Both events lead to the same effect an augmentation of the ratio between the length of the muscle in the contracted and the distended state expressed in percentage of the total fiber length

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and an asynchronism of the electrical events at the end of ventricular repolarization that are responsible for the U wave An earlier similar asynchronism is the cause of the T wave The duration of the action potential in one region is different from that in another and the first region stimulated need not be the first to be repolarized so that there is an asynchronism of events So I contend as has Schaefer that in the future the U wave must be correlated to such asynchronism I must say however that, while the U wave may be an exciting detail to study I am not sure that it has very much practical importance in electrocardiographic diagnosis today except in the recognition of the effects of electrolytes and quinidine

L LEPESCHKIN The one thing that possibly may be bothering us is the significance of the inverted U waves as an isolated finding This has involved quite a discrepancy of opinion I think that 99 per cent of the cases have some cardiac pathology usually left ventricular hypertrophy or some type of coronary heart disease but occasionally people sixty to seventy years of age show isolated U waves without developing any other clinical symptoms I should like to have Katz s opinion concerning this

L N KATZ We too have seen these isolated inverted U waves but apparently not as frequently as Holzmann[33] so that we are not inclined to ascribe too great a clinical importance to them I think such discrepancies in observation depend upon the criteria of normality and abnormality and these vary from one group to another Perhaps we should follow Schmitt s suggestion namely that we check our ability to interpret the same curves as unknowns from time to time and see how closely we approach the old interpretation Further it would be interesting to take the same set of electrocardiograms and send it to half a dozen different schools of electrocardiography to see how they agree or disagree in their interpretation

References

1 WEIDMANN S 1955 Elektrophysiologie der Herzmuskelfaser Huber Bern Switzerland

2 TINGL E L V WOODBURY & H H HECHT 1952 Effects of innervation and drugs upon direct membrane potentials of embryonic chick myocardium J Pharmacol Exptl Therap 104 103

3 LEPESCHKIN E 1951 Modern Electrocardiography 1 Williams & Wilkins Baltimore Md

4 LEPESCHKIN E 1955 The U wave of the electrocardiogram A M A Arch Internal Med 96 500

5 FURBETTA D A BUFALARI & P SANTUCCI 1955 La Parte Finale del Ventricologramma (Onda U e Tratto TU) e la Sindrome dei Muscoli Papillari Universo Rome Italy

6 LEPESCHKIN E 1952 Observations on the genesis of the U wave of the electrocardiogram Federation Proc 11 92

7a SEGERS M 1941 Le potentiel consécutif négatif dans le coeur Compt rend soc biol 135 409

7b SEGERS M 1941 Le rôle des potentiels tardifs du coeur Mém acad roy méd Belgique 1(7

8 BOZLER E 1943 Tonus changes in cardiac muscle and their significance for the initiation of impulses Am J Physiol 139 477

9 BROOKS C McC B F HOFFMAN E E SUCKLING & O ORIAS 1955 Excitability of the Heart Grune & Stratton New York N Y

10 SJOSTRAND T 1951 After potentials in the electrocardiogram Acta Physiol Scand 24 247

11 GOLDMAN D E 1943 Potential impedance and rectification in membranes J Gen Physiol 27 37
12 SHANES A M H GRUNDFEST & W FREYGANG 1953 Low level impedance changes following the spike in the squid giant axon before and after treatment with veratrine alkaloids J Gen Physiol 37 39
13 SHANES A M 1949 Electrical phenomena in nerve I Squid giant axon J Gen Physiol 33 57
14 SHANES A M 1949 Electrical phenomena in nerve II Crab nerve J Gen Physiol 33 75
15 SHANES A M 1951 Potassium movement in relation to nerve activity J Gen Physiol 34 795
16 SHANES A M 1952 The ultraviolet spectra and neurophysiological effects of veratrine alkaloids J Pharmacol E ptl Therap 105 216
17 FRANKENHAEUSER B & A L HODGKIN 1956 The after-effects of impulses in the giant nerve fibers of *Loligo* J Physiol 131 341
18 HODGKIN A L & R D KEYNES 1955 Active transport of cations in giant axons from *Sepia* and *Loligo* J Physiol 128 28
19 SHANES A M 1957 Ionic transfer in a vertebrate nerve *In* Metabolic aspects of transport across cell membranes Univ Wisc Press In press
20 SHANES A M 1954 Effect of temperature on potassium liberation during nerve activity Am J Physiol 177 377
21 SHANES A M 1952 Ionic transfer in nerve in relation to bio-electrical phenomena Ann N Y Acad Sci 55(1)
22 FLECKENSTEIN A & A HARDT 1949 Der Wirkungsmechanismus der Lokalanasthetika und Antihistaminkorper—ein Permeabilitatsproblem Klin Wochschr 27 360
23 DUDEL J & W TRAUTWEIN 1954 Das Aktionspotential und Mechanogramm des Herzmuskels unter dem Einfluss der Dehnung Cardiologia 25 344
24 ARVANITAKI A 1938 Proprietes Rhythmiques de Matiere Vivante Hermann Paris France
25 LEPESCHKIN F B SURAWICZ & H HERRLICH Unpublished observations
26 NAHUM L H & H E HOFF 1939 The interpretation of the U wave of the electrocardiogram Am Heart J 17 585
27 SURAWICZ B & E LEPESCHKIN 1953 The electrocardiographic pattern of hypopotassemia with and without hypocalcemia Circulation 8 801
28 SCHERF D & A SCHOTT 1953 Extrasystoles and Allied Arrhythmias Heinemann London England
29 COVINO B G & L WILLIAMS 1955 Excitability cycle of the ventricle in hypothermia Am J Physiol 181 362
30 SZENT GYORGYI A 1952 Contraction in the heart muscle fiber Bull N Y Acad Med 28 3
31 HAJDU S 1933 Mechanism of staircase and contracture in ventricular muscle Am J Physiol 174 371
32 SCHAEFER H 1951 Das Elektrokardiogramm Theorie und Klinik Springer Verlag Berlin Germany
33 HOLZMANN M & W ZURUKZOGLU 1955 Die klinische Bedeutung der negativen und diphasischen U Wellen im menschlichen EKG Cardiologia 27 202

THE PHYSIOLOGICAL BASIS OF THE SPREAD OF CARDIAC ACTION CURRENTS THROUGH THE BODY

By L. N. Katz

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The preceding section was concerned with the manner in which electric currents are created in living tissues and how they spread from one part of the heart to another, as well as with the mechanisms involved. In this part of the monograph we shall consider the results of the fact that the heart, like all living cells of the body except those in the skin, lies within a volume conductor.

In order to put this subject into its correct perspective I should like to refer to Hecht's recent editorial in *Circulation Research*[1] in which he pointed out that Lord Kelvin, as far back as 1840, presented mathematical formulas with which he could take boundaries into consideration in trying to arrive at the effects of dipoles within a conducting medium and that by 1852 Helmholtz had the mathematics of volume conductors fairly well worked out. We must also give credit at this time to Craib and Canfield who, while working with Sir Thomas Lewis in London, oriented the electrocardiographic picture into the framework of a volume conductor.[2] Then Wilson and his school[3] as well as Bayley[4] worked out the application of Helmholtz's concepts in more detail. Later on you will learn from F. D. Johnston (who is heir in residence of Frank Wilson) and R. McFee about the newest development in this subject.

I believe the purpose of this part of the monograph can be characterized best by posing a few questions. Since the heart lies within the body, the electrical manifestations of its activity will be modified by the electrical properties of the body acting as a three dimensional conductor. I have little patience with those who think that consideration of the manifest value in a single plane is enough. It is as if one considered two dimensional pictures to be a complete reproduction of a three dimensional world. This volume conductor is finite, not infinite. It is nonspherical and it is inhomogeneous. Furthermore, the heart is located eccentrically and it is close to the surface. These are the things I used to stress in the 1930s. I am pleased that they are being stressed again now.

How far do these factors alter the deductions obtained for an infinite (or a large spherical and finite) homogeneous conductor in which no phase boundaries exist and in which the current source is a fixed tiny centrally placed dipole? How far can these differences between ideal and actual situations be predicted by theory and calculation and models? How far can we get with speculations and impressive long formulas and to what extent must they be determined by actual trial on living human subjects? How much information must we obtain first by observation before deriving the formulas? What is the range of variability among normal subjects resulting from differences in physique and the position, anatomy and physiology of the heart? You have

read in Part II for example how the opinions of Medrano *et al* and of Scher and Young have differed concerning the spread of the impulse in the ventricular septum Is this due to a difference in technique in deduction or is it merely the variability in the animals that were used? Also what about man? Is the physiology the same in all of us or does it vary noticeably? Furthermore do facts derived from studies on normal subjects apply to diseased subjects in whom the characteristics of the body the heart and their interrelationships are so much more variable than in healthy persons?

Despite all the efforts in developing the concept of the volume conductor very little has been done with diseased hearts—hearts with infarcts dilated hearts hypertrophied hearts variously displaced hearts and hearts displaced closer to the chest wall

How far does inhomogeneity influence the spread of cardiac currents throughout the body? What are the influences of the body boundary (which has recently been receiving a great deal of attention) and of phase boundaries? What is the role of the eccentricity of the dipole equivalent, which is not always in the heart s center? These are all very important questions

Furthermore can the electrical events of the heart cycle be reduced reasonably to a dipole equivalent? This is only an assumption The heart is the size of the fist It has a septum and free walls and the impulses move through it in a very complex topographical fashion There is a junction between the active and the inactive parts of the heart giving rise to a theoretical surface for which a vector can be substituted Can one synthesize all this reasonably into one dipole and how reasonably? Also is that dipole fixed or does it shift in a very complicated fashion during the heart cycle?

Are there proximity potentials on the surface of the body and what is their extent? Protagonists of vectorcardiography like to view the subject of projection of electrical activity upon the body surface in a global manner in which differences with respect to the distances between the heart and the electrodes do not have too great importance Very recently however Hartmann *et al*[5] reported that when a cat s heart was put into a fish bowl filled with saline and when the potentials were explored in this homogeneous field proximity potentials became very significant as soon as the exploring electrode approached the heart to a distance equal to or twice its diameter If proximity potentials do come into play then how can we accept an oversimplified concept?

What is the quantitative influence of all of these numerous variables? While we read these pages we must ask ourselves constantly Is this for an idealized dream world or is this for the real world in which we actually live? Only by consideration of all these variables in health and disease and surely with the aid of theory models and mathematics can the problem of the spread of the current of the heart through the body ultimately be solved A good beginning has been made

Finally it is important to emphasize that the existence of controversy indicates that the subject matter is in its beginnings that it is still unsettled When the controversy is resolved and the facts are established conferences such as the one upon which this monograph is based will not be needed Stu

dents will be taught the facts routinely and we investigators will embark on a search for new knowledge elsewhere

References

1 Hecht H H 1955 Editorial Research in electrocardiography Circulation Research 3 231
2 Craib W H & F Canfield 1927 A study of the electrical field surrounding active heart muscle Heart 14 71
3 Wilson F N A C Macleod & P S Barker 1933 The distribution of currents of action and of injury displayed by heart muscle and other excitable tissues Univ Mich Studies Scientific Series 10 Univ Mich Press Ann Arbor Mich
4 Wilson F N & R H Bayley 1950 The electrical field of an eccentric dipole in a homogeneous conducting medium Circulation 1 84
5 Hartmann F K Vearat O A M Wass & F W Duchosal 1955 Vectorcardiography as studied on the isolated mammalian heart suspended in a homogeneous volume conductor Cardiologia 27 129

THE SPREAD OF CURRENTS AND DISTRIBUTION OF POTENTIALS IN HOMOGENEOUS VOLUME CONDUCTORS*

By Franklin Davis Johnston
University of Michigan Medical School Ann Arbor Mich

Frank N Wilson struggled for several years during the 'twenties to convinc physicians and physiologists that laws governing the flow of currents and th distribution of potentials in volume conductors must be applied to electro cardiography In 1932 he had already completed a long basic paper largel devoted to this subject and this was published as a monograph by the Un versity of Michigan Press the following year[1] Several of the figures used t illustrate my brief discussion of the matters under consideration have bee taken from that monograph

FIGURE 1 indicates that A Waller in the last century, had a good concept o the distribution of currents and potentials arising from the heart In th figure voltages produced by the heart are represented by two poles of a batter A and B and a few of the infinite number of paths of current flow are indicate by the fine dotted lines The solid lines surrounding pole A and the dashe and dotted lines close to pole B represent regions of equal potential Thus A is the positive and B the negative pole of the battery all points on eac dashed and dotted line are equally positive in potential and all points on eac solid line are equally negative in potential It may be pointed out that a vecto collinear with the current axis through A and B may be used to represent th magnitude and direction of the electromotive force (E M F) of the batter and that a line drawn perpendicular to the line joining the poles of the batte at its mid point that is the zero potential line should be an excellent referen point for the measurement of potential anywhere in the medium

Before the Einthoven triangle concept and subsequent developments a discussed a few words should be said about some of the mathematical expre sions that may be employed to determine the potential of any point in volun conductors of different kinds Such expressions are available only for hom geneous conductors of simple types and some of these are shown in FIGURE 2 EQUATIONS 1 and 2 apply to a plane lamina infinite in extent and EQUATION applies to a circular lamina of radius R EQUATIONS 4 and 5 apply to a hom geneous medium of infinite extent in all directions and (6) applies to a spheric medium of radius R For the derivation of these equations the intereste reader is referred to the monograph of Wilson and his associates[1] mention above

During the 1920s when Wilson was working to prove that laws pertaini to the flow of currents in volume conductors must apply to electrocardiograph

* Support for studies presented in this article has been provided by a grant to Frank Wilson by the S S Kresge Foundation Detroit Mich and funds have also been provid by the Michigan Heart Association Detroit Mich and the National Institutes of Heal Public Health Service Department of Health Education and Welfare Bethesda Md (H 5114)

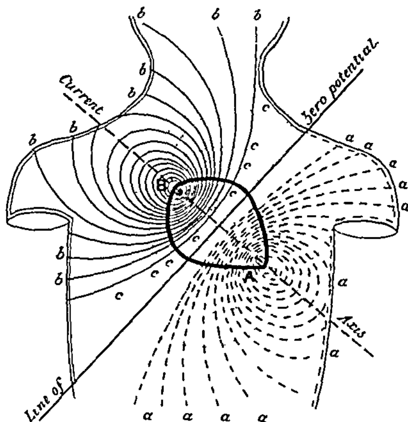
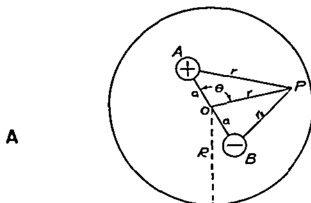


FIGURE 1. *A* and *B* are 2 points of the apex and base, respectively. A straight line between *A* and *B* represents the axis of current between *A* and *B* if any inequality of potential should arise between the two points. The dotted lines (*c*) represent lines of current diffusion, the broken lines (*a*) represent equipotential lines surrounding the point *A*, and the continuous lines (*b*) represent equipotential lines surrounding the point *B*. A straight line at right angles to the current axis represents the line of zero potential.

Craib[2,4] was engaged in similar studies employing strips of cardiac and skeletal muscle and medullated nerve fibers. The results of Craib's studies were published before Wilson had completed all of his work, but the opinions of the two workers on opposite sides of the Atlantic Ocean were in harmony. In this connection Wilson[1] wrote: "In stating that work on the general subject of this monograph was begun in this laboratory a number of years before Craib's first paper was published (see Wilson, Wishart and Herrmann, 1926[5] and Wilson, 1930[6]) and that many of the facts to which he has called attention were known to one of us long before that paper appeared, we do not wish to raise any question of priority or in any way to claim any share of the credit due Craib for the fine work he has done. Inasmuch as our work has been done independently of his, we have naturally followed our own point of view. Craib's work has, however, made it unnecessary for us to carry out experiments



$$V = \log_e \frac{r_2}{r_1} \qquad (1) \qquad\qquad V \quad \left(- - \frac{1}{r_1} \right) \qquad (4)$$

$$V = 2ae \frac{\cos\theta}{} \qquad (2) \qquad\qquad V = 2ae^2 \frac{\cos\theta}{r^2} \qquad (\ )$$

$$V = 2ae\cos\theta \left(\quad + \frac{}{R} \right) \qquad (3) \qquad\qquad V = 2ae^2\cos\theta \left(- + \frac{2}{R} \right) \qquad (6)$$

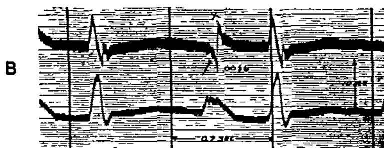


FIGURE 2 In FIGURE 2B the *top curve* represents a direct lead from a point on the surface of the auricle of a la ge dog midway between the upper end of the sulcus terminalis and the tip of the right auricular appendix An upward deflection indicates the relative negativity of the exploring electrode The indifferent elect ode is on the left hind leg Ten mv equals 2 cm The deflection time of the string for 10 mv is about 0 0028 sec There is slight overshooting and the string is not quite aperiodic The duration of the intrinsic auricular deflection is about 0 0036 (Lucas comparator) The *lower cu ve* represents the exploring electrode near the junction of the superior vena cava and the right auricle possibly on the vein The indifferent electrode is on the right hind leg (Reproduced by permission of the University of Michigan Press Ann Arbor Mich)

upon simple tissue strips or to enter at length upon subjects that have been adequately discussed in his papers

It is clear from the above that Wilson was in full agreement with the work Craib had done with muscle strips and other simple preparations and it re mained only to prove that laws governing the flow of currents in volume con ductors applied equally to the mammalian heart beating in the experimental animal To accomplish this essentially unipolar electrocardiograms (FIGURE 2B) were recorded midway from the upper end of the sulcus terminalis to

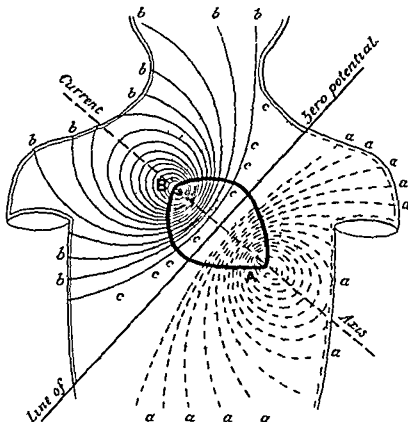


FIGURE 1 A and *B* are 2 points of the apex and base respectively. A straight line between A and *B* represents the axis of current between A and *B* if any inequality of potential should arise between the two points. The dotted lines (*c*) represent lines of current diffusion the broken lines (*a*) represent equipotential lines surrounding the point A and the continuous lines (*b*) represent equipotential lines surrounding the point *B*. A straight line at right angles to the current axis represents the line of zero potential.

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in a different way the same information seen in the scalar leads 1, 2 and 3 It should be emphasized that the limb leads the Einthoven triangle arrangement and the vectorcardiogram shown in FIGURE 6 are concerned with components of cardiac voltages in the frontal plane

Supposing that the assumption underlying the Einthoven triangle is strictly true Wilson and his associates[7] showed in the early 1930s that a network by

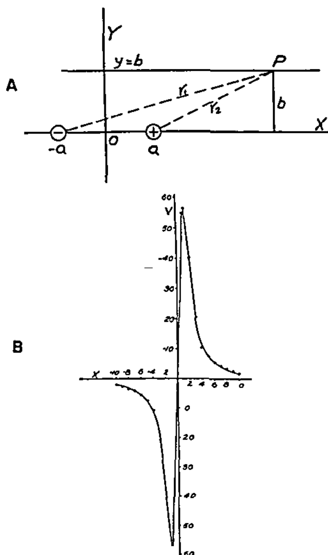


FIGURE 3 Reproduced by permission of the University of Michigan Press Ann Arbor Mich

which the electrodes on the right arm left arm, and left leg are connected to a common point through equal resistances of at least 5000 ohms established an indifferent electrode with small potential variations throughout the cardiac cycle FIGURE 7A shows this scheme in diagrammatic form Wilson fully appreciated the inaccuracies of the central terminal electrode but he believed that it served as the best indifferent electrode available for the registration of

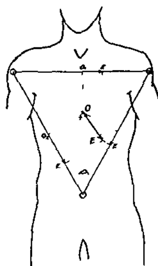
A

B

$$I = \frac{4c\,\mu(x+a)}{\sqrt{(x+a+s)^2+b^2}}\int \frac{d\phi}{\sqrt{1-k^2\sin^2\phi}} - \frac{4c\,\mu(x+a)}{\sqrt{(x-a+s)^2+b^2}}\int_0 \frac{d\phi}{\sqrt{1-k_1^2\sin^2\phi}}$$

C

FIGURE 4 Reproduced by permission of the University of Michigan Press Ann Arbor Mich



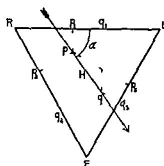


FIGURE 5

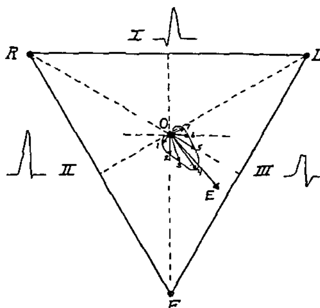


FIGURE 6 Reproduced by permis ion of W B Saunders Co Philadelphia Pa

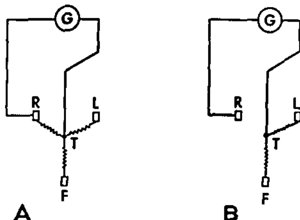
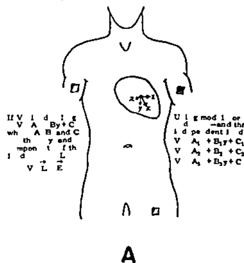


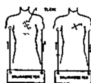
FIGURE 7 Reproduced by permission of F A Davis Co Philadelphia Pa

nearly unipolar precordial leads and further that it provided an electrode with such small voltage changes that it could be used to obtain tracings that represented approximately at least the potential variations of the extremities A few years later Goldberger[8] pointed out the modification of the central terminal circuit needed to take augmented unipolar extremity leads (FIGURE 7B) (aV_R aV_L and aV_F) and thereafter so-called unipolar electrocardiography assumed the place it holds today

I have often wondered if Wilson was not somewhat surprised at the nearly universal acceptance of the central terminal technique In any event he fully appreciated and welcomed the lead vector concept when it was first described by Burger and van Milaan[9, 10] about ten years ago This idea is very important since it provides a tool for the determination of the behavior of any lead free of most of the restrictions imposed by the assumption that underlies the Einthoven triangle

Since the lead vector has served as the basis for much important work in the last few years and has been perhaps a somewhat difficult concept for the average physician a few words describing it are in order In FIGURE 8A the voltages in the heart are represented by a single equivalent dipole the size and direction of which are represented by the vector E This vector may be replaced of course by its three orthogonal components x y and Suppose vector E has a purely transverse direction in which case the y and z components are zero Under these circumstances the voltage produced by E (or x) in any bipolar lead (for example lead 1) is Ax where A is a constant or coefficient that involves matters such as inhomogeneity of the tissues and the spatial relations between the E M F (Ex) and the electrodes of the lead employed Similarly if the direction of E is purely vertical the transverse and sagittal components x and z are zero and the lead voltage V is By where B is again a constant coefficient that describes the reaction of the lead in question to a vertically oriented voltage located at a specified point in the heart If these conditions are true by the superposition theorem the lead voltage V is equal to $Ax + By + Cz$ Burger and van Milaan further pointed out that the coefficients A B and C may be considered as the x y and z components of a





$\frac{E}{I} = \frac{i}{I}$ (1)

$I = \frac{i}{E}$ (2)

$I = \frac{V}{R}$ (3)

$I = \frac{E}{R}$ (4)

$\frac{V}{R} = \frac{i}{I\ R}$ (5)

$V = \frac{i}{I}$

if $I = 1$
$V = i$

A

B

FIGURE 8 FIGURE 8B is reproduced by permission of Grune and Stratton Inc New York N Y

vector *which is the lead vector L* and this fully describes the performance of a particular lead It should be emphasized that for a given lead determination of the coefficients A B and C establishes the behavior of the lead for only a single position of the equivalent dipole in the heart If the dipole is moved these coefficients may change appreciably Burger and van Milaan also showed that the lead voltage V equals the scalar product of the lead vector L and the vector E that represents the equivalent dipole in the heart Thus V equals $\overrightarrow{L}\overrightarrow{E}$

It is not possible to estimate the coefficients that establish lead vectors directly in man but Burger and van Milaan and many other workers more recently by the use of models or of cadavers have determined them for many commonly used leads in approximate fashion This is possible since voltages of known size and direction can be introduced into the cardiac area of the model and if the voltage produced in a lead is measured with the dipole oriented successively in the x y and z directions 3 equations with only 3 unknowns A B and C are available and these can be solved for the coefficients Thus in the equation $V_1 = Ax$ where V_1 is the lead voltage the dipole of known strength is oriented in a strictly transverse manner Under such circumstances y and z are zero and the general equation reduces to $V_1 = Ax$ Orientation of the dipole in the vertical and sagittal directions gives the equations $V_2 = By$ and $V_3 = C$ and allows calculation of B and C If the lead vectors are known for 3 independent leads either in models or man the size and direction of the equivalent cardiac dipole can be calculated Thus the equations

$$V_1 = A_1x + B_1y + C_1z$$
$$V_2 = A_2x + B_2y + C_2$$
$$V_3 = A_3x + B_3y + C_3z$$

where V_1, V_2, and V_3 are known lead voltages and A_1, B_1, C_1, etc. are the known lead vector coefficients for the respective leads, can be solved for x, y, and z, the 3 orthogonal components of the vector E.

The concept of the lead field has been described in detail by McFee and Johnston.[11, 13] It is not an entirely new concept, since the tubes of influence mentioned by Lepeschkin[14] represent essentially the same idea. The lead field depends entirely on the reciprocity theorem of Helmholtz; consequently it is essential that this theorem be clearly understood. In his derivation of the reciprocity theorem, Helmholtz was considering the effect of an electromotive surface in a volume conductor on the deflection of a galvanometer connected to that conductor. He stated the theorem in the following way:[15] "Every single element of an electromotive surface will produce a flow of the same quantity of electricity through the galvanometer as would flow through that element itself if its electromotive force were impressed on the galvanometer wire. If one adds the effects of all the electromotive surface elements, the effects of each of which are found in the manner described, he will have the value of the total current through the galvanometer."*

Referring to FIGURE 8B, an element of the electromotive surface in the heart, e, will produce the same current in the external galvanometer circuit as would flow through the element e were its voltage impressed on the galvanometer circuit. This reciprocal relationship is expressed in more general terms by the equation $\frac{E}{e} = \frac{i}{I}$ (EQUATION 1 in the figure), where e, as before, is the voltage of the element in the heart, E is the voltage impressed on the galvanometer circuit, i is the current through the element in the heart, and I is the current in the galvanometer circuit. EQUATION 2, $I = \frac{ie}{E}$, is EQUATION 1 rearranged and solved for I. By Ohm's law, the current I in the galvanometer circuit equals the lead voltage V divided by the total resistance between the 2 electrodes, R. Thus EQUATION 3 is $I = \frac{V}{R}$. If another battery of voltage E is impressed in the galvanometer circuit, it is clear that the current in the galvanometer circuit now becomes EQUATION 4, $I = \frac{E}{R}$. If the values for I in EQUATION 3 and for E in EQUATION 4 are substituted in EQUATION 2, the following expression is obtained: $\frac{V}{R} = \frac{ie}{IR}$ or $V = \frac{ei}{I}$. Finally, if the voltage of the battery in the external circuit is altered so that unit current is introduced into the lead, I becomes 1 and the final equation (5) is $V = ei$. This is the basic expression in the lead field concept, and it states that the voltage in any lead due to an electromotive element in the heart equals the product of this element e and the current that passes through the element if unit current is introduced into the lead. This idea may be extended to all elements of electromotive force in the heart. Thus in

$$V = e_1 i_1 + e_2 i_2 + e_3 i_3 + \ldots \qquad (6)$$

* Wilson made this clear and concise translation from Helmholtz's original paper.

where V is the open circuit voltage of a lead the e's are the potential differences of the electromotive force elements and the i's are the currents passing through the elements when a unit current is introduced into a lead

If unit current is introduced into the two electrodes of any lead currents will flow through all parts of the body, including the heart since at any point in the body the current will have a certain direction and magnitude it may be considered as a vector field and be represented by $\vec{J}$ where the magnitude of $\vec{J}$ is measured in terms of current per unit area at every point If the electromotive surfaces considered in the previous paragraph are very small the current field will be uniform over the whole element and the total current passing through it will be the product *of the component of the field perpendicular to the surface* of the element and its area By the fundamental equation (5) of the lead field $V = ei$ the voltage produced in the lead by this element will be the product of this total current and the potential difference of the element If we now define the electromotive vector $\vec{e}$ of any small element of electromotive surface as a vector that points in the direction faced by the positive side of the element, and that has a magnitude equal to the potential difference across the element multiplied by its area then $V = \vec{J}\,\vec{e}$ or $V = J_x e_x + J_y e_y + J_z e_z$ It will be observed that these equations for the lead voltage are the same except for some difference in the symbols employed as those relating to the lead vector and it is clear that the lead field for any point in the heart is identical to the lead vector for that point EQUATION 6 above may now be written

$$V = \vec{J}_1\,\vec{e}_1 + \vec{J}_2\,\vec{e}_2 + \vec{J}_3\,\vec{e}_3 + \cdots$$

and thus the essentially algebraic lead vector may be replaced by the more geometric and physical concept of the lead field

It must be made clear at this point that the lead field is determined by the currents that flow through the body (including the heart) When an external battery of proper size is connected to the electrodes of any lead however this does not in any way alter the basic fact that voltages originating in the heart are responsible for electrocardiograms obtained when a suitable recording instrument is connected to those electrodes Further it must be emphasized that the part of the lead field passing through the heart is the only portion that is important in electrocardiography The lead field is actually a device that helps in understanding the behavior of any lead and the design of new and better ones The following illustrations should aid in making its value clear

In FIGURE 9A the approximate lead field for lead 1 is illustrated *Here the* heart is represented by the shaded area and it will be observed that the current field produced by the external battery that is the lead field passes in a generally transverse direction through the heart This means that lead 1 depicts fairly well transverse components of voltages arising in the heart This should be clear from the previous discussion of the nature of the lead field but consideration of FIGURE 9B may make this even more obvious Here a single element of the lead field and 2 sources of voltage or dipoles A and B in the

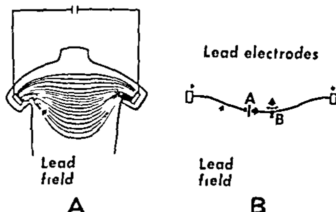


FIGURE 9 Reproduced by permission of F A Davis Co Philadelphia Pa

heart both located on this element are shown Source A is oriented with its positive and negative poles parallel to the lead field and it contributes *in the greatest possible degree* to the lead voltage Source B on the other hand is oriented with the positive and negative poles at right angles to the lead field and it contributes *nothing* to the lead voltage

The implications of the above should be clear Although it is not possible to determine the exact path of the lead field through the myocardium fortunately intuition and common sense enable us to establish its approximate course through the heart by the use of simple spatial relationships between the locations of electrodes and the heart The lead field thus provides a simple and powerful tool not only to explain how any type of lead will function but even more important to indicate what types of electrodes or electrode systems should be employed to obtain leads that are ideal for specific purposes

In FIGURE 10A we see a representation of the lead field for lead aV$_F$ obtained from a fluid mapper as described by McFee *et al*[16] It is a hydraulic analog to the electrical situation in the human subject for the lead mentioned Here water enters the orifice in the left leg flows upward in a shallow space and passes out in equal amounts through orifices in the two arms Paths of fluid flow are visualized by small crystals of soluble dye and the flow of currents (the lead field) through the human body would be similar if a battery were connected to the terminals of lead aV$_F$ It will be observed that the field is reasonably uniform and nearly vertical in direction This suggests that this would be a satisfactory lead for obtaining the vertical component of cardiac voltages

The ideal unipolar lead from the lead field standpoint is one in which the field radiates symmetrically in all directions from the exploring electrode to the indifferent electrode (at infinity) The field obtained with a fluid mapper set up to represent a unipolar chest lead employing the central terminal is shown in FIGURE 10B Here fluid passed into the model *in equal amounts* through orifices in the two arms and left leg and out through an opening over the cardiac area This nearly perfect field may be contrasted to the one obtained for a CR chest lead (FIGURE 10C) Here fluid (or electricity) passes

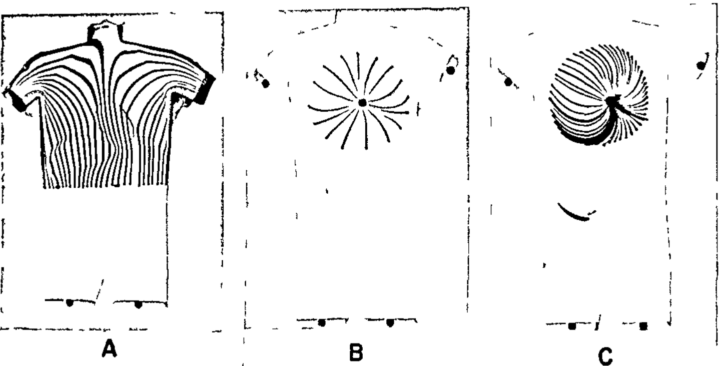


FIGURE 10 FIGURES 10A and 10B are reproduced by permission of Grune and Stratton Inc New York N Y

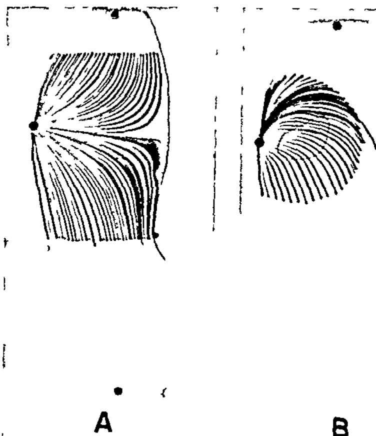


FIGURE 11

from a single orifice (or electrode) in the right arm and out through the aperture (or exploring electrode) over the heart FIGURES 11A and 11B respectively illustrate sagittal views of the fields obtained with a chest lead employing the central terminal and the same chest lead where the leg was used as the indifferent electrode (CF lead) It will be noticed that in the former the field radiates in quite symmetrical fashion from the exploring electrode and that there is concentration of the field in the anterior parts of the heart The latter must mean that leads of this kind are more sensitive to voltages on the anterior than on the posterior aspect of the heart

I wish now to emphasize a point that should by now be obvious The lead field concept makes clear the type of field that must exist in the heart if a lead is to be ideal for vectorcardiography Thus for the best possible transverse vertical and sagittal components of the cardiac E M F s the fields (associated with the leads employed) must be like those shown in FIGURE 12 *a* *b* and *c* respectively The type of electrode system required to obtain a good sagittal

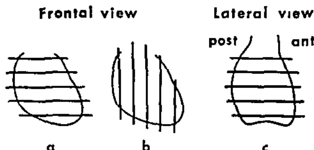


FIGURE 12 Reproduced by permission of F A Davis Co Philadelphia Pa

component and its associated lead field are shown in diagrams *a* and *b* respectively of FIGURE 13B Several small electrodes each connected through large equal resistances to a common electrode are placed over the precordial areas anteriorly and posteriorly The number of electrodes necessary to ensure that the lead field will be satisfactory will vary somewhat with heart size and with other factors At the moment it seems likely that a minimum of fifteen electrodes well distributed over the precordium and a somewhat fewer number posteriorly should be provided The smaller the number of electrodes used especially anteriorly the more critical their placement will be The advantage of the multiple electrode grid arrangement for obtaining the sagittal component of cardiac E M F s is shown very clearly in FIGURE 13A where the lead field for this system is contrasted with those that exist with the so called cube and the tetrahedron arrangements Although the lead field for the latter has an average anterior posterior direction there is considerable curvature of the field indicating that lead V_B (employed for the tetrahedron system) is sensitive to vertical as well as to sagittal components of the heart voltages Furthermore this lead is more sensitive to voltages on the posterior than on the anterior aspect of the heart The lead field for leads employed with the cube arrangement shows marked curvature when it is remembered that the electrodes for this lead are located on the lower chest near the *right* anterior and

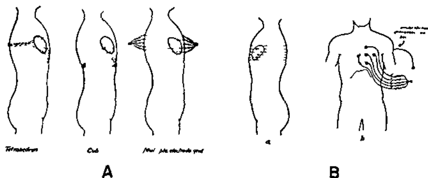


FIGURE 13 Methods of obtaining a good sagittal component (FIGURE 13A is reproduced by permission of Grune and Stratton Inc New York N Y)

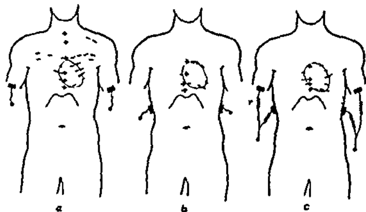


FIGURE 14 Reproduced by permission of Grune & Stratton Inc New York N Y

posterior axillary lines it will be clear that this arrangement records transverse and vertical components of cardiac voltages as well as sagittal components

Finally in FIGURE 14 a simple arrangement for improving the behavior of lead 1 if it is to be used for the transverse component of a vectorcardiogram is shown Thus although the lead field for lead 1 alone (FIGURE 14a) has a general transverse direction the curvature particularly near the apex impairs the accuracy of the lead for the purpose at hand If however a lead with electrodes in the midaxillae slightly below the level of the heart (FIGURE 14b) is combined through large resistances with lead 1 (FIGURE 14c) the opposite curvature of the fields in *a* and *b* will tend to cancel each other giving a resultant field with a more purely transverse direction

This brief discussion of the lead field is incomplete in many respects but it will furnish I hope some indication of its power and simplicity

In summary I have tried to outline some of the basic considerations relating to the distribution of currents and potentials in homogeneous volume conductors, including the use made of some of these matters by Einthoven, Wilson and others The lead vector of Burger and van Milaan has been briefly described and a somewhat more detailed discussion of the lead field has been given

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I wish to make it clear that the lead field concept and its development have been almost entirely the work of Richard McFee and to him must go the credit for this fine contribution I am also indebted to several of my present and former associates for helping in the collection of some of the material presented in this paper These include Ernest W Reynolds Jr Robert M Stow Jerome F Cordes and Park W Willis III My debt to Frank N Wilson in so many ways is so great that I can find no words to express it

References

1 WILSON F N A G MACLEOD & P S BARKER 1933 The distribution of the currents of action and injury displayed by heart muscle and other excitable tissues Univ Mich Press Ann Arbor Mich

2 Craib W H 1927 A study of the electrical field surrounding active heart muscle Heart 14 71

3 Craib W H 1928 A study of the electrical field surrounding skeletal muscle J Physiol 66 49

4 Craib W H 1930 The electrocardiogram Med Research Council Brit Spec Rep Series No 147

5 Wilson F N, S W Wishart & G R Herrmann 1926 Factors influencing the distribution of potential differences produced by heart beat at the surface of the body Proc Soc Exptl Biol Med 23 276

6 Wilson F N 1930 Distribution of the potential differences produced by the heart beat within the body and its surface Am Heart J 5 599

7 Wilson F N, F D Johnston, A G Macleod & P S Barker 1934 Electrocardiograms that represent the potential variations of a single electrode Am Heart J 9 447

8 Goldberger E 1942 A simple indifferent electrocardiographic electrode of zero potential and a technique of obtaining augmented unipolar extremity leads Am Heart J 23 483

9 Burger H C & J B van Milaan 1946 Heart vector and leads I Brit Heart J 8 157

10 Burger H C & J B van Milaan 1947 Heart vector and leads II Brit Heart J 9 154

11 McFee R & F D Johnston 1953 Electrocardiographic leads I Introduction Circulation 8 554

12 McFee R & F D Johnston 1954 Electrocardiographic leads II Analysis Circulation 9 255

13 McFee R & F D Johnston 1954 Electrocardiographic leads III Synthesis Circulation 9 868

14 Lepeschkin E 1951 Modern Electrocardiography Williams & Wilkins Baltimore Md

15 Helmholtz H 1853 Über einige Gesetze der Vertheilung elektrischer Ströme in körperlichen Leitern mit Anwendung auf die thierisch-elektrischen Versuche Ann Physiol Chem 29(3) 222

16 McFee R, R M Stow & F D Johnston 1952 Graphic representation of electrocardiographic leads by means of fluid mappers Circulation 4 21

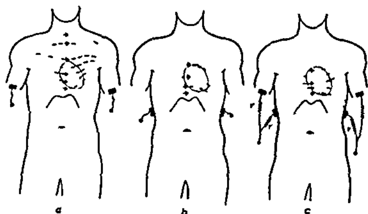


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in the first category with a considerable amount of electrophysiology both experimental and theoretical Here the scope of the problem is broader than in the first category and it appears that our knowledge in this area is less fully developed than in category No 1 Category No 3 presents another shift in emphasis and enters a still more complex area Here it becomes necessary to supply the final link between initial surface potentials and the ultimate answers sought from them taking into account the multiplicity of information that can be obtained from a wide variety of clinical tests of the condition of the heart Although the separation among these categories cannot be and is not as sharp as outlined it is profitable nevertheless to examine this gross structure in order to appreciate the interrelation of the subdivisions Close cooperation and collaboration among all specialized workers is vital for maximum effectiveness in the pursuit of the over all goal

The Fundamental Problem

This paper deals with theoretical and experimental findings in category No 1 As such it does not of course produce any final answers to the over all problem The intent is to summarize and integrate the present state of knowledge in this category to stress some of the basic ideas and to provide a background for future research Historical developments in this area cannot be sharply traced principally because this category had not been decisively recognized in the past and had not been crystallized as an aid to study More over much of the past work that can be fitted into this category was not started with a sufficiently fundamental point of view and oversimplifications were frequently introduced too early in the process Furthermore available concepts and tools were not fully recognized and exploited

The fundamental problem which defines category No 1 may be stated as follows *Given a three dimensional conducting medium with an insulating boundary (the human body) and a time varying potential distribution over the boundary (P QRS and T waves) determine the characteristics of internal electrical generators that could have produced this potential distribution* Merely stating the problem reveals much about its nature when reflecting upon our general knowledge of potential theory First and most important it is found that an answer to this problem is possible but that a unique answer is fundamentally impossible It is known that potential distributions on the boundary do not specify unambiguously internal generators that produced the potential distributions A simple example of this is found in the one dimensional case of electric circuit theory It can easily be shown that for a device with two terminals across which a potential difference exists an infinite number of different internal generators could have produced this same potential difference In the case of the three dimensional system no restrictions are placed on the number of boundary points at which potentials can be measured This constitutes a system with an infinite number of terminals and one might legitimately ask Does the accessibility to an infinite number of terminals accomplish a uniqueness absent in the one dimensional case? Fortunately this basic question has long been settled but, unfortunately for electrocardiography the answer is that internal

SPREAD OF CURRENT IN VOLUME CONDUCTORS OF FINITE EXTENT*

By Ernest Frank†

Moore School of Electrical Engineering, University of Pennsylvania, and the Robinette Foundation, Hospital of the University of Pennsylvania, Philadelphia, Pa.

Introduction

The complexity of electrical activity in the human heart that gives rise to electric currents that course through the elaborate structure of the human torso and produce potential differences on the irregularly shaped body surface poses a challenging problem in electrocardiography. Attempts indirectly to deduce information concerning the heart from conveniently accessible body surface potentials have shown the problem to be of such complexity and diversity that specialists in various aspects have emerged. Separation of the over-all problem into less formidable subdivisions has been a logical course to follow. It is a typical pattern found in all scientific pursuits dealing with problems of this nature. While there is a risk of excluding pertinent items because of the artificiality of such subdivision, meaningful progress can result within each category if choice of compartmentalization is sound. Blending and integrating information from each subdivision to reconstruct the whole may then give more comprehensive and more complete results than would have been possible without the artificial compartmentalization.

Subdivisions of the over-all problem of electrocardiography that appear thus far to be useful choices include the following three categories: (1) the relationship between body surface potentials resulting from electrical activity in the heart and an equivalent generator that could have produced these same potentials, (2) the relationship between the equivalent generator and the actual electrical activity in the heart, and (3) the relationship between the detailed electrical activity in and the condition of the heart.

These categories not only partition the problem into three convenient areas for separate study, but they also possess some other notable features. They are logical subdivisions since they represent three stages of thought process that may be applied in interpreting body surface potentials measured on the human subject. Moreover, each category represents a problem of a rather distinct nature which emphasizes different aspects of the over-all problem and suggests the training and background of specialists who might work fruitfully in each area.

Category No. 1 represents a problem that is almost entirely physical and mathematical, and deals with potential theory concepts that have been widely developed and applied successfully to a wide assortment of problems. In one sense it represents the simplest of the three subproblems. Category No. 2, judged to be second in order of complexity, is one that blends ideas involved

* The work reported in this article was supported in part by Grant H 339 C from the National Institutes of Health, Public Health Service, Department of Research Grants and Fellowships, Bethesda, Md.

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generators still cannot be established uniquely despite access to an infinite number of terminals It can be shown that for any given three dimensional potential distribution it is always possible to add current sources and sinks inside the medium in such a way that the boundary potential is unaffected This means that viewed the other way around there is no way to establish purely from surface measurements a unique internal generator

This indicates a salient limitation of electrocardiography An equivalent generator that by definition produces exactly the same body surface potentials as the actual heart generator can be deduced from body surface potential measurements but there is an infinite number of different equivalent generators that could produce this same result It follows that the equivalent generator does not necessarily bear a literal resemblance to the actual generators within the heart since the heart generator is unambiguous physically This leads to another important idea The equivalent generator is no more than a conceptual entity It does not exist physically It merely represents a fictitious generator that could have produced the observed electrical effects

The Dipole Concept

Having defined the fundamental problem and realized the inherent limitations of the hypothetical equivalent internal generator the next question is What approaches are useful for determining equivalent internal generators for the human heart? One approach to this problem utilizes some general theorems of potential theory It can be shown in principle that the surface (vector) integral of the potential over the entire boundary can be utilized to deduce the nature and location of internal equivalent generators [1] Application of this idea to the human subject is extremely difficult and elaborate but it is basically sound in principle An alternative approach that is easier to implement follows a method used widely in science namely first to explore the simplest possible explanations of observed phenomena

The very simplest current generator is the so called dipole defined as a positive point source and an equal negative point source with separation between sources approaching zero while maintaining constant the product of source strength times separation This current generator called mathematically a double singularity is a hypothetical entity and a mathematical concept but one that can be approximated physically if desired [2] It is conveniently representable by a vector of magnitude equal to the dipole moment (product of source strength times separation) of direction along the line joining the two sources and having a sense from the negative toward the positive source With this fictitious generator one may attempt to account for the boundary potential produced by the actual heart generator It may seem fruitless to consider the simple dipole as a serious candidate for an equivalent representation of the enormously complicated activity in the human heart It is useful to explore this possibility fully however if for no other reason than to find a direction for future work Potential theory indicates that the dipole is at least a first approximation in a problem of this type There is also some theoretical evidence that this simplification might apply with considerable accuracy [3]

Theory of Dipole Potentials

A straightforward procedure may be used to ascertain the applicability of this simplest kind of equivalent generator to boundary potentials produced on the human body surface by the actual heart generator A theory is developed in rather general terms for dipole potentials in bounded media and a sensitive method is then evolved from this theory for testing its applicability to the actual physical system This procedure is characteristic of the type of approach that has been so successful in many other scientific investigations, but it does not exclude other possible theories

In order to keep the development within manageable complexity it is desirable to place some reasonable restrictions on the electrical characteristics of the medium These must not be incompatible with measured characteristics of the human body The assumptions are that the medium is (1) resistive and (2) linear These assumptions have ample experimental support[4,6] and it is likely that they will stand indefinitely as progress continues in this field Applicability of the resistive property relies in no small measure on the fact that heart frequencies are confined to reasonably low values and the linear property rests on the fact that heart current densities within the medium are not excessive It is important to appreciate that these restrictions are relatively mild for the development of this theory since the medium may have any shape and there is no requirement that it be homogeneous

To develop the theory consider a dipole located at any arbitrary *fixed* point within a resistive linear three dimensional medium of any boundary shape and select any two points on the boundary For convenience a rectangular coordinate system may be used to describe the system as indicated in FIGURE 1 First consider a single dipole oriented along the direction of the x axis The potential difference produced between the two boundary points will be proportional to the dipole moment because the medium is resistive and linear that is if the dipole moment is doubled the potential difference between the two boundary points is doubled This may be expressed in equation form as $V = c p$ where V is the potential difference between the two arbitrarily chosen boundary points p is the moment of the x oriented dipole and c is a constant of proportionality

This simple statement embodies the essence of the entire theory and therefore deserves some detailed examination particularly in connection with the constant of proportionality c which will be seen later to be the x component of the so called image vector With some reflection it becomes clear that c depends upon the electrical characteristics of the medium and also upon the boundary points between which the potential difference is measured for if the medium is changed in any way (as to resistivity distribution or kind of inhomogeneity or shape) c will change Moreover if the medium characteristics are held constant but the boundary points for potential measurement are changed the value of c will vary with choice of boundary points It is further evident that the constant c will also depend upon the location of the internal dipole The potential difference however will always be proportional to the dipole moment p for any given medium given pair of boundary points and fixed di

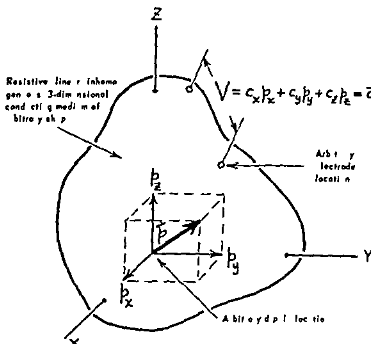


FIGURE 1 General bounded conducting medium with the immersed current dipole $\vec{p}$ of rectangular components p p and p

pole location Thus this equation partitions the effects due to the dipole moment itself from those due to the parameters of the system It represents a neat means for distinguishing between electrical aspects of the generator and quantities pertaining to the remainder of the system and it is exactly what is desired

For a dipole located at the same point and oriented along the direction of the y axis the potential difference between the same boundary points will be of the same essential character that is proportional to the dipole moment which can be symbolized by p_y in this case with some different constant of proportionality c_y So the potential difference produced in this case is ex pressed by the equation $V_y = c_y p_y$ In similar fashion the potential difference produced by a z-oriented dipole can be formulated as $V \; = c \; p$ In each of these three cases the constants c c_y and c depend upon the medium charac teristics (size shape resistivity distribution of inhomogeneities) the dipole location and the location of the two boundary points

Since the medium is linear the superposition principle may be applied to deduce an expression for the potential difference that will be produced between the two boundary points when all three dipoles are present simultaneously by simply adding the contributions of each dipole separately The result is evi dently

$$V = c \; p \; + c_y p_y + c \; p \tag{1}$$

In this form the three orthogonal dipoles of moment p p_y and p may be regarded as components of a dipole vector $\vec{p}$ of arbitrary orientation Also a vector $\vec{c}$ may be defined that has orthogonal components c c_y and c, and is called the image vector (or lead vector) This enables a vector interpretation of EQUATION 1 $V = \vec{c} \cdot \vec{p}$ The potential difference V may be thought of as arising from the dot (or scalar) product of the dipole vector $\vec{p}$ and the image vector $\vec{c}$ These are the beginning and fundamental ideas of a dipole theory in which the concept of vector projection may be employed[7, 7] Development of this theory has been presented fully elsewhere[8]

Equivalent Heart Dipole

One of the important consequences of this theory is that the existence of exact mirror patterns (measured with respect to any arbitrary reference point formed by the junction of two or more resistors connected to two or more boundary points) is predicted for a fixed location dipole whose moment and orientation vary with time[9] This property of the boundary potentials suggests a precision method for ascertaining the applicability of the fixed location equivalent dipole representation of human heart activity A technique using four electrodes on the human body has been developed in which mirror patterns are sought and canceled against each other in what is essentially a bridge circuit[9] Electrodes 1 and 2 shown in FIGURE 2 are connected through a pair of resistors to form a convenient and arbitrary reference junction R Mirror patterns are sought at two other electrodes 3 and 4 with respect to this junction by a systematic procedure These patterns are then canceled against each other compensating for unequal amplitudes by means of adjustment T The technique represents a generalization and clarification of that used by Schmitt and his co-workers[10] If the fixed location dipole theory were exactly applicable to human body surface potentials exact mirror patterns would be found experimentally with corresponding perfect cancellations Furthermore if cancellation is good but not perfect then the degree of cancellation is a quantitative measure of the applicability of the fixed location dipole hypothesis[9] Failure to obtain perfect cancellation in practice as in FIGURE 3 may be attributed to effects other than nondipolar potentials Some of these include mobility of the dipole during the complex under study atrial depolarization effects and such practical factors as inadequate posture and respiration control of the subject and nonthoroughness of experimental search

Results of extensive studies of this type on many humans both normal and abnormal have been presented for the QRS complex[9, 13] Much more experimental work must be done before final conclusions are reached and evidently more time must elapse before the full significance of the results is appreciated So far it appears that the single fixed location dipole hypothesis is applicable to the QRS complex to an accuracy of 85 to 95 per cent with a tendency for more accuracy in normals than in individuals with certain types of heart disorders Records in FIGURE 3 indicate 95 per cent applicability for the electrode sites under test Some preliminary work on T wave cancellation in normals[14] indicates that the dipole approximation may be equally applicable No stud

ies have been made of the P wave using this technique. The results are especially remarkable when one considers the many varied factors cited that can contribute to the noncanceling result and that are charged against the dipole hypothesis.

The literature contains details of equipment, procedures, and experimental results, but it is worth while here to emphasize the significance of this information. Some far reaching fundamental consequences in the field of electrocardiography are implied. The first and most obvious conclusion is that if body surface potentials are dipolar in nature, the problem of category No. 1 becomes a relatively simple one of determining components of the equivalent dipole. This reverts, then, to the problem of determining suitable coefficients (or image vectors) for the human subject, as can be seen from EQUATION 1 where measurement of I with knowledge of $\vec{c}$ for three independent leads enables $\vec{p}$ to be established.[8] Thus, efforts to determine human coefficients deserve emphasis, for they are stepping stones to the equivalent dipole of the human heart.

A second important consequence of dipolar potentials is that they make it

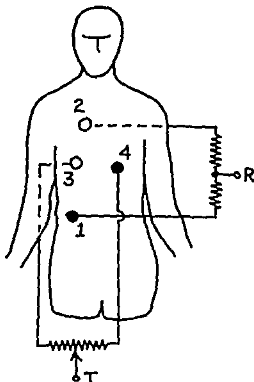


FIGURE 2. Four-electrode cancellation technique useful for testing the dipole hypothesis on intact human subjects. The body search with electrodes 3 and 4 for mirror patterns with respect to reference junction R permits a small residual potential to be achieved between A and the adjustable tap T of the potentiometer.

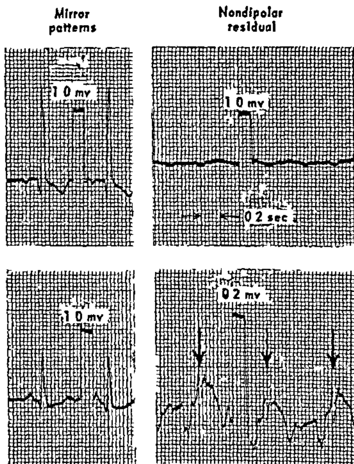


FIGURE 3 Representative mirror patterns (left) at electrodes 3 and 4 of FIGURE 2 (one has been recorded with reversed polarity for convenience in comparing wave shapes) are seen to cancel almost completely in the record on the upper right which is the potential difference between *R* and *T* A highly amplified record of the canceled result is shown at the lower right Vertical arrows indicate the nondipolar content of the QRS complex Note that P and T waves do not cancel under these same conditions

possible for vectorcardiography to rest on a firm physical foundation Equivalent dipole applicability implies that there are only three independent generator quantities necessary to describe surface potentials over the entire body the three dipole components This means that in principle any three independent potential differences will give all available information and that additional leads will give only redundant information Hence three correctly designed vectorcardiographic leads can give a physically meaningful result But this would not be the case if the dipole hypothesis were inapplicable To clarify this point further suppose the heart were not representable by an equiv

alent dipole It would still be possible to measure three independent potential differences record 'vector' loops and interpret the heart 'dipole Much could probably be learned experimentally on this basis This would be an empirical approach, however The pseudodipole being dealt with would not have an intimate relationship to electrical events in the heart and would thereby be fundamentally limited The important distinction to recognize is that the equivalent dipole assumes a deeper physical significance when body surface potentials are actually (or very nearly) dipolar and opportunity for physical theory is opened with the reduction of limitations inherent in any empirical method To exploit fully the possibilities of vectorcardiography it is necessary of course to obtain an accurate quantitative determination of the equivalent dipole which is not being achieved with most systems in current use

A third important conclusion that stems from the single dipole applicability is rather unfortunate from a clinical point of view If the very simplest generator a dipole can account for the bulk of available surface potential information this corresponds to a minimum amount of heart generator information available from the body surface If potentials on the body surface did have a substantial nondipolar content then more information concerning the equivalent generator than three quantities would be necessary and *determinable* from the surface measurements by procedures more complicated than vector cardiography It is obvious that the proximity potential concept falls in this latter category but experimental findings of mirror pattern cancellations *undermine this possibility*[9] *Admittedly it would be extremely valuable* clinically to glean information concerning local regions of heart muscle that are close to an exploring precordial electrode but this is a fleeting hope that melts in the face of experimental facts

A final implication of the dipole result is that there is no basic information obtained by the use of a reference potential of any kind (derived from body surface electrodes) that cannot be found in bipolar leads No new independent data are contributed by such a reference terminal since its potential is derived from the electrodes to which it is connected and the electrode potentials in turn are predictable from the equivalent dipole This does not imply that use of a reference terminal of some sort might not have certain practical experimental advantages or might not possess some clinical merit empirically this has indeed been found to be the case for the Wilson central terminal But it should be clearly recognized that a reference terminal constitutes a device of convenience rather than one of basic value Indeed the same is true in the nondipolar case

Broad consequences of equivalent dipole behavior underscore the need for extensive and careful work in further explorations of its applicability Fortunately practical equipment and techniques for doing this on a wide scale have been developed The deep significance of the results cannot be ignored It should be emphasized that the dipole concept and tests of its applicability to the human rely in no way on model studies involve no assumptions whatsoever concerning the shape of the human torso do not require the medium to be homogeneous and do not restrict the fixed location of the equivalent dipole

It is astonishing that such far reaching fundamental conclusions can be reached with so few basic assumptions

Parameters that Influence Dipole Potentials

The surprising degree to which potentials on the human body are compatible with an equivalent internal dipole suggests that it is desirable to study proper ties of dipole potentials in bounded media in more detail Such studies are multipurposed and they have revealed many results that can serve at least as a guide for future research some of them appear useful for incorporation into clinical practices Several objectives are suggested below

(1) To ascertain the degree to which the simple idealizations embodied in present day clinical electrocardiography depart from physical facts Specifi cally what are the effects of removing the currently used assumptions of a spherical conductor to represent the body and a dipole location at the center of the sphere?

(2) To determine the importance of various electrical and physical param eters of the over all system such as the location of the dipole the shape of the boundary and the electrical characteristics of the medium in so far as they influence boundary potentials produced by an internal dipole

(3) To explore methods of establishing suitable coefficients (components of image vectors) for the human subject, so that components of the human heart dipole may be determined quantitatively on the living subject

(4) To become sufficiently acquainted with the over all problem to assess the feasibility of implementing quantitative procedures that are practicable clinically

While this list is far from complete it suggests some of the comprehensive objectives of such studies Since the entire emphasis in all of this work in category No 1 is directed toward quantitative results the first aspect to recog nize is that all studies must involve the behavior of dipole potentials in three dimensional media This is because dipole potentials in three dimensional media and seemingly similar two-dimensional cases (such as sphere and circular disc) are not quantitatively the same While many investigators have used two dimensional theoretical and experimental approaches fruitfully to reach qualitative conclusions that have enhanced our appreciation of the kind of problems with which we are confronted the situation is now in a state where one can no longer be satisfied with this kind of result Although electrocardiog raphy has been satisfactory in the past on a pictorial and descriptive basis recognition of the potentialities of quantitative methods must be appreciated to permit further advances

Theoretical studies Studies of parameters that influence dipole potentials on the boundary of three dimensional conducting media have been carried out in both theoretical and experimental directions Theoretical analyses have of necessity been more restricted than experimental work because only rather simple media and boundaries can be handled mathematically without excessive complication Nevertheless such theoretical work has been valuable in point ing to several critical items Analyses of eccentric dipoles in homogeneous

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spherical media[18, 19] have been useful to show that location of the dipole has a very significant effect on boundary potentials. Comparison of dipole potentials produced in homogeneous three dimensional media of various shapes such as the sphere[19] the finite length cylinder[20, 21] the infinite length cylinder[22] and the prolate spheroid[23] reveal that boundary shape influence is not overly critical. These investigations alone show that heart vector methods based on the simplified theory of Einthoven are in a semiempirical category that represents a mathematical device that cannot be quantitatively correlated with electrical effects in the heart although such methods do serve a useful empirical purpose in the clinical interpretation of the electrocardiogram.

Model studies. A more realistic approach involves experimental studies utilizing three dimensional models of the human torso with an immersed dipole (FIGURE 4). Extensive work has been done with such models by several investigators[7, 7, 24, 25]. The principal advantages of the experimental approach

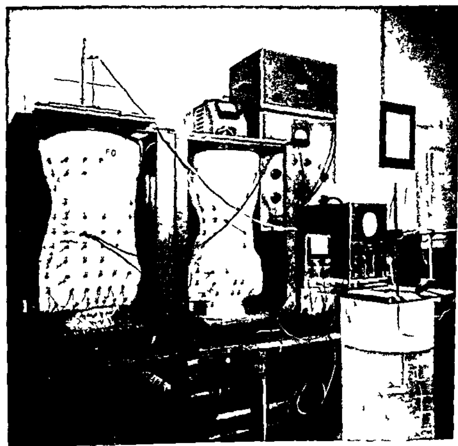


FIGURE 4. Three dimensional male and female life size torso models with the associated apparatus used to study parameters that influence dipole potentials (photo courtesy of Chas Pfizer & Co Inc Brooklyn N Y)

have been the ability to use a more suitable boundary shape and also to introduce inhomogeneities into the medium Both of these items are difficult if practicable at all to accomplish by mathematical analysis This approach entails the immersion of a finite dipole (whose moment location and orientation are known) into the model and the measurement of boundary potentials produced by the dipole The electrical system can be studied conveniently at leisure Everything about the system is accessible and can be measured quantitatively Some of the broad conclusions of model studies are

(1) The influence of dipole location on surface potentials is extremely pronounced and dipole location is the most sensitive parameter of the entire system[19, 26] To illustrate if a dipole placed in a life size model produces a potential distribution over the boundary a slight location change of 1 cm changes the boundary potentials by as much as 20 per cent

(2) The influence of torso shape is present but is a less important factor than dipole location[19, 27] Indeed once a rough torso shape has been established then deviations corresponding to a reasonably wide range of body builds result in relative changes in potential of the order of 10 per cent Even when a cylinder shape is used the boundary potential is still quite similar quantitatively to that produced on a torso shaped model[28]

(3) The influence of inhomogeneities introduced into the model is much less than might be expected especially when the inhomogeneities are located reasonably distant from the dipole The image vector coefficients determined by Burger and van Milaan[7, 7] on an inhomogeneous model agree within several percentage points with those determined independently on homogeneous models[8] On the other hand inhomogeneities very close to the dipole can exert considerable effect on potential distribution at the boundary As a practical matter however this effect appears to be inextricably tied in with the equivalent heart generator and will be discussed more fully later

(4) The relationship between anatomic points and electrical effects is not simple and is strongly dependent on dipole location[29] Anatomic axes are generally not parallel to the effective electrical axes and anatomic distances are very deceptively related to electrical amplitudes (FIGURE 5)

While the above four items represent the essence of the over all conclusions there is available a tremendous amount of detailed information that gives some idea of the errors of current methods Some of the prominent errors deserve mention here

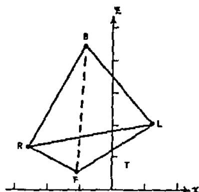
(1) The limb lead triangle for a three dimensional torso model with an internal dipole can be seen in FIGURE 5 to depart markedly from the equilateral triangle of Einthoven[27] The model triangle is scalene it is considerably elongated in the head to foot direction it is not parallel to the anatomic frontal plane and lead I slants backward and upward from the horizontal One consequence of these results for the QRS complex is illustrated in FIGURE 6

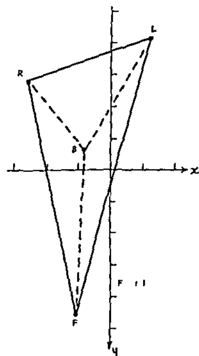
(2) The front to back component of the dipole can contribute significantly to limb lead potentials[27] In cases where this component is sizable in the human subject deceptive results can be expected when this effect is ignored

(3) The Wilson central terminal potential departs from the dipole mid poten

tial in typical cases by 30 per cent of the value of the maximum frontal plane potential[27]

(4) The left arm potential is quite unreliable quantitatively because it depends critically on the left shoulder structure the left shoulder being attached to the body over a region of very steep potential gradient owing to the leftward and forward location of the dipole[30]





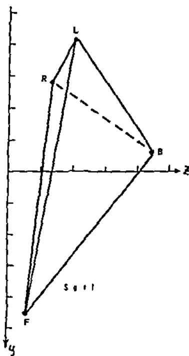


FIGURE 5 Geometric representation of the electrical distortion effects due to the torso shape and eccentric dipole location for the standard limb electrodes R L F and the Wilson back electrode B in terms of the image vectors associated with these leads The dipole location is at the origin of the coordinate system

(5) Commonly used systems of vectorcardiography are seen to possess sizable errors on the models[26,31] Lead vectors of such systems as the cube double cube and tetrahedron (FIGURE 5) are not parallel to anatomic axes are not mutually perpendicular or equal in length and are strongly dependent on dipole location

Model studies evidently reveal the rather severe inadequacies of present methods in so far as quantitative work is concerned especially since current method of analysis of electrocardiograms and vectorcardiograms rely on the assumption of a fixed location dipole in a homogeneous medium

Applicability of Models to Humans

Theoretical and model studies of the influence on dipole potentials of various parameters of the system such as torso shape dipole location, and medium inhomogeneities contribute to a quantitative appreciation of the nature of the system It cannot be assumed without proof however that model behavior is directly applicable to the human subject While the dipole hypothesis itself can be and has been tested without recourse to models further tests on human subjects are necessary to establish the degree to which model behavior is quantitatively useful for humans

The difficulty of testing the applicability of models to the human subject

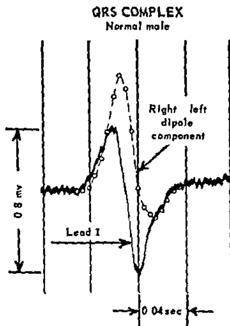


FIGURE 6 Deceptive clinical result may be seen in the high speed record of lead I on comparison with the accurate research determination of the right left component p (dashed lines joining small circles) The discrepancy between lead I and p is traceable to the lead I image vector which in this case slants backward and upward from the horizontal by 17

can be seen immediately when one considers the extreme sensitivity of surface potentials to dipole location.[26, 27] Model studies reveal that it is pointless to *attempt quantitative correlation without an accurate knowledge of the physical* location of the equivalent dipole of the human subject. To overcome this serious obstacle, a precision method was devised using a cancellation principle (similar to that used for the dipole applicability test) to determine this most important parameter.[19] The technique entailed obtaining numerous cancellations among pairs of electrodes located at the mid ventricle level around the entire chest of the human subject and fitting these data with those derived from corresponding points around a homogeneous model with an immersed dipole of known location. Since a cancellation technique was used, it was not necessary to know the actual dipole components of the subject to execute the method. The dipole location in the model that resulted in the best fit of model and human data was taken as the location of the equivalent dipole in the human subject. While the method is not perfect, being molested by inhomogeneity effects, the chest contour fit was sufficiently satisfactory to proceed. For the first normal subject studied, the location of the equivalent dipole for the QRS complex was established to within ±0.5 cm, and dipole mobility was found to be less than 1/2 cm. This data fitting method is far superior to an integration method that has been suggested[1] and it has been carried out on a wide variety of subjects using model data that have been published expressly for this purpose.[19]

With a known dipole location it is possible to make a detailed point by point comparison of potentials on the human subject with those at corresponding points on the homogeneous model. This may be done most precisely by a cancellation technique. It may also be carried out in terms of QRS wave forms since knowledge of dipole location for the individual subject enables the dipole components to be determined. In essence, the entire procedure amounts to obtaining a best fit between model and human over a critical region of steep potential gradient and then testing for agreement at points scattered over the entire torso.

A portion of the results of these experiments in terms of QRS complexes and instantaneous equipotentials over the entire body surface[30] is illustrated in FIGURES 7 and 8. The essential results for the entire body surface were that quantitative agreement within ±15 per cent was found to exist between the amplitude and shape of the QRS complexes of the human subject and the potentials produced at corresponding points on the homogeneous model by an immersed fixed location dipole. The significance of this quantitative statement can be appreciated from the typical record in FIGURE 9, in which the amplitude and shape agreement is 13 per cent. The experimental demonstration that model predictions apply to the human with quantitative accuracy when the dipole location and torso shape are properly taken into account indicates that it is feasible to devise quantitative methods of vectorcardiography based on the behavior of homogeneous three dimensional torso models.

The methods and techniques employed in this critical experiment indicate that the applicability of model to human may be expected to be comparable to that obtained in the extensive and complete research experiment mentioned above for each individual in whom a successful determination of dipole location

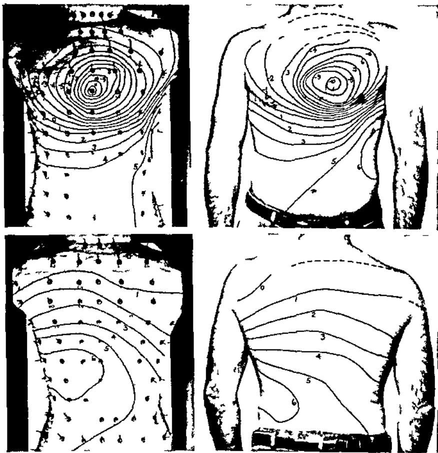


FIGURE 7 Absolute comparison of instantaneous equipotentials at the time of the R wave peak in lead II for a normal QRS complex and dipole in a homogeneous model The potential difference between the adjacent equipotentials is 0 25 mv The dipole orientation is downward backward and to the left (reproduced from Circulation Research 1955 3 243)

has been carried out Successful determinations have been obtained in forty cardiac patients[13] The conclusion of quantitative model applicability to the human subject therefore has considerable breadth This is not surprising because the subject tested initially was arbitrarily chosen and a *principle* rather than specific individual characteristics was being tested

Clinical Implementation

Culmination of work in category No 1 with the positive conclusion that it is quantitatively feasible to determine the equivalent dipole for the QRS complex of the human subject is of course not the end of the matter The methods employed in the research investigations were elaborate and required special

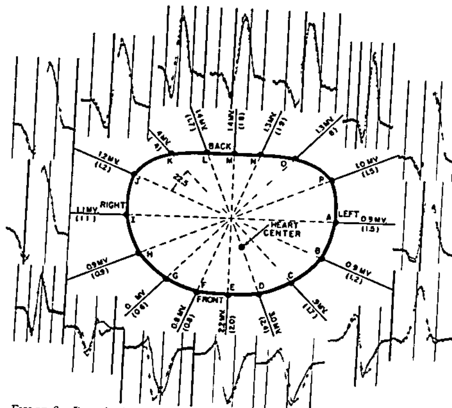


FIGURE 8 Records of unipolar potentials during the QRS complex measured with respect an accurate tailored 2 resistor terminal for 16 electrode locations (A through P) around the chest of a normal male subject The calculated points shown on each record by small circles at 18 instants spaced 0 005 sec apart are based on the homogeneous torso model coefficients with the optimum dipole location for this subject Each record was made simul taneously with lead II (not shown) for time synchronization Measured amplitudes in milli volts are indicated on the radial lines along with the corresponding calculated amplitudes in parenthesis The calculated wave forms are drawn equal in peak to peak value to the corre sponding record for shape comparison (reproduced from The American Heart Journal 1955 49 670–692)

equipment and time-consuming techniques The next question to be faced is Are there clinically practical methods of obtaining this quantitative result? This question has been the object of pursuit of numerous groups around the world The principal obstacle is dipole location which has been found to differ considerably among various individuals [13] Once the dipole location has been determined for an individual subject dipole components can readily be obtained Dipole location is not easily established with required accuracy however and a clinically practicable procedure has not been forthcoming

An alternative is to devise a method of dipole component determination that is relatively insensitive to dipole location To some extent this can be done by using carefully selected groups of electrode sites joined through appropriate networks in which dipole location effects tend to offset one another [23]

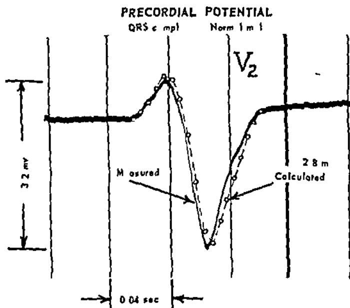


FIGURE 9 Enlarged version of a record similar to tho e shown in FIGURE 8 for an electrode location at a slightly different anatomic level

Devising such leads does not remove the restrictions of a fixed location equivalent dipole a trap into which one might easily fall It is interesting that this same objective of invulnerability to dipole location has been sought on the basis of lead field concepts in terms of a uniform reciprocal lead field through the heart volume[34 34a] Concepts of lead vectors and lead fields are fundamentally the same One can be derived from the other by use of the reciprocity theorem which is valid because of the linearity of the medium[35] It follows that the same fundamental limitations exist for both concepts and it is unfortunate that some groups have been led to the erroneous conclusion that a uniform lead field through the heart enables the single fixed location dipole hypothesis to be circumvented What it does achieve is invulnerability to the location of the single equivalent dipole

A system of orthogonal leads invulnerable to dipole location that strikes an optimum compromise among many conflicting factors has been devised It has the advantages of a sound theoretical and physical basis insensitiveness to individual variability of dipole location reasonable speed and ease of application corrections for the shape of the human torso better signal to-noise ratio than in remote electrode systems exclusion of the left arm electrode with its attendant errors and a cost comparable to that of other systems This system shown in FIGURE 10 employs seven electrodes (three on the precordium) and has been in use for almost a year It embodies all of the pertinent findings of research studies of the problem A detailed description of this system is available[36] It is too early to determine whether or not im

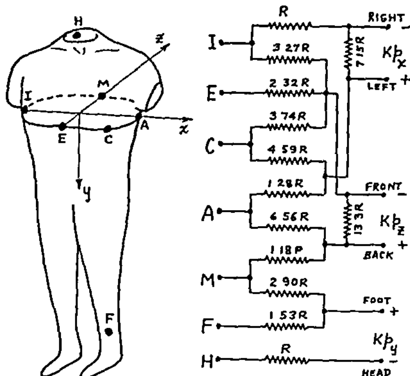


FIGURE 10 Seven electrodes of a proposed system of vectorcardiography affixed to the human subject at the left The precise electrode locations are described elsewhere[1] Computing and compensating networks (right) correct for torso shape and dipole location and produce 3 outputs proportional to the dipole components p p and p with equal standardization for the dipole locations within a 5 by 5 cm area at the midventricle level The networks have been designed to have equal resistance levels to combat 60 cps interference The recommended value of R is 50 000 ohms to avoid appreciable body loading

proved accuracy with ability to quantitate results will be useful clinically but the more accurate anteroposterior dipole component produced by this system illustrated in FIGURE 11 in itself represents a marked improvement over systems currently used[37]

While the problem initially posed in category No 1 is by no means completely solved a substantial amount of progress has been made and the course for future development in this area is clearly indicated Some items for future work include

(1) Further and exhaustive studies of the applicability of the fixed location dipole hypothesis to human subjects Such studies should include the T wave as well as the QRS complex Eventually it might be desirable to study the P wave but this is the most difficult of the three to examine with present techniques

(2) Additional determinations of anatomic locations of the equivalent dipole for both the QRS complex and T waves especially in the same individual[14] The difference between these locations in the same individual has a strong

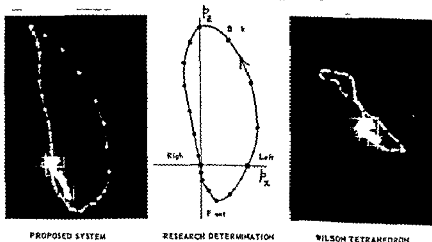


FIGURE 11 Projections of vector loops in the transverse (x) plane for a normal male subject recorded with the system of FIGURE 10 and also with the Wilson tetrahedron are compared with an accurate research determination of the QRS loop The disagreement of the tetrahedron result is excessive in this case The rectangular grid line spacing in the records is 0 1 inch The standardization employed in the proposed system was 1 inch/mv fo both components and in the Wilson system it was 1 inch/mv for lead I an 1 1 2 inch/mv for V_E The timing markers in the records are spaced 2 5 msec The bright spots occur immediately after blanked portions of trace and reveal the direction of inscription The points on the research determination are spaced 5 msec apart

practical bearing on methods of quantitative electrocardiography of the future and may be of considerable significance in the concept of ventricular gradient

(3) Further investigation[33] of independent methods for determining image vector coefficients for the human subject that can then be compared with the present model technique

(4) Detailed quantitative investigation of a host of practical factors relating to clinical implementation such as the study of electrode sites with reproducibility and sensitivity to dipole location in mind and the study of left arm characteristics in terms of the steep potential gradient at the left shoulder

Although the seven electrode system of vectorcardiography shown in FIGURE 10 represents a reasonable answer to these problems that seems satisfactory at the moment there is no reason to believe that further improvement is not possible

Some Fundamental Questions

In the course of work in category No 1 several significant basic questions have arisen The first deals with the equivalent dipole and its fixed location which have been found consistently by direct experiment on a wide variety of subjects There is little doubt that both of these properties are applicable

for the QRS complexes of many humans although detailed information concerning ventricular depolarization as learned in category No 2 seems to conflict with the single fixed location dipole representation especially with respect to the fixed location There is theoretical evidence that the single-dipole equivalent might be expected despite the size and eccentric location of the heart as long as there is one continuous double layer in the myocardium[8] When the wave of depolarization separates into several islands in various parts of the heart however as in the later stages of ventricular depolarization one might expect the single dipole idea to become impaired Moreover even in the case of a single continuous double layer its travel through the heart implies a corresponding equivalent-dipole motion estimated to be about 2 or 3 cm although less than one half cm travel is indicated in terms of boundary potentials[19] and greater mobility would show up in a very pronounced manner with the sensitive technique employed

A plausible explanation for this seemingly conflicting set of results can be offered in terms of internal short-circuiting effects within the heart which contains blood of approximately ten times the conductivity of the external medium *Because internal short circuiting effects have not been studied experimentally* this explanation is offered as a speculation It appears that internal effects would tend to pull the heart together electrically so to speak into a much smaller entity than its physical size indicates One reason why this speculation seems promising is that it would explain qualitatively at least both of the difficulties that is both the dipole behavior and the fixed location would tend to become more and more applicable as the volume interior to the heart was increased in conductivity This is regarded as a pertinent area for future study in order to reconcile all experimental findings However, it belongs in category No 2 since it deals with one aspect of the correlation between the equivalent generator obtained from the boundary and detailed activity in the heart The complexity of category No 2 is revealed by this speculation since it shows that local inhomogeneities as well as detailed electrical activity in heart muscle might be necessary properly to interpret the equivalent dipole

A second closely related question immediately becomes apparent Is it not likely that the equivalent dipole determined from the boundary is considerably influenced by local inhomogeneities that seriously warp the boundary view of electrical activity of heart muscle despite corrections for torso shape dipole location and other parameters? Are not the components of the equivalent dipole no matter how accurately determined still distorted representations of the electrical generator? Some investigators would suggest that this local inhomogeneity effect[39] should be charged against the accuracy with which the equivalent dipole has been determined that is against the lead vectors However it would seem logical to keep this problem in category No 2 It is informative to note that the influence of inhomogeneities within and close to the heart is not ruled out by the homogeneous model experiments mentioned previously It may well be that these inhomogeneity effects have been charged against the dipole components and must eventually be untangled before an undistorted electrical view of the heart can be obtained

A third fundamental question deserves mention because some investigators

have been attempting work in this connection Is it fundamentally po ible to determine image vector components *exclusively* from measurements on the body surface of the human subject? It is known that these coefficients can be determined approximately by using model comparisons[32] as well as internal dipoles placed within the subject[39] Can we look forward to the time when it will be pos ible to carry out independent determinations on the intact subject? It would appear to be fundamentally impossible to achieve this result The basic reason can be found in the linear relation EQUATION 1 which exists for any lead and which involves three coefficients that it would be necessary to determine Each time a new lead is introduced experimentally, three additional unknown coefficients appear but only one more lead voltage is measurable There appears to be an insufficient amount of independent data to determine the coefficients *solely* from boundary potential measurements This appears to be true even in the case of a planar dipole loop[40] Since the impossibility has not been proved rigorously but is only strongly suspected it can be said only that one should strongly question the basic validity of any experiments that claim that coefficients have been determined *exclusively* from boundary potential measurements

References

1 GABOR D & C V NELSON 1954 *Determination of the resultant dipole of the heart from measurements on the body surface* J Appl Phy 25 413
2 FRANK E 1955 Esophageal dipole design J Appl Physiol 8 305
3 FRANK E 1953 A comparative analysis of the eccentric d uble layer representation of the human heart Am Heart J 46 364
4 GOLDSTEIN H L C F KAY & H P SCHWAN 1953 Phase shift in body tissues as it pertains to electrocardiography Federation Proc 12 53
5 SCHWAN H P C F KAY P T BOTHWELL & E L FOLTZ 1954 Electrical resistivity of living body tis ues at low frequencies Federation Proc 13 131
6 KAUFMAN W & I D JOHNSTON 1943 The electrical conductivity of the tissues near the heart and its bearing on the distribution of the cardiac action currents Am Heart J 26 42
7a BURGER H C & J B VAN MILAAN 1946 Heart vector and leads Brit Heart J 8 157
7b BURGER H C & J B VAN MILAAN 1947 Heart vector and leads. Part II Brit Heart J 9 154
7c BURGER H C & J B VAN MILAAN 1948 Heart vector and leads Part III Geometrical representation Brit Heart J 10 229
8 FRANK E 1954 General theory of heart vector projection Circulation Research 2 258
9 FRANK E 19 5 Measurement and significance of cancellation potentials on the human subject Circulation 11 937
10 SCHMITT O H R B LEVINE E SIMONSON & J DAHL 1953 Electrocardiographic mirror pattern studies Parts I II III Am H art J 45 416 500 655
11 MOORE S R & P H LANGNER JR 1956 Location of the electrical center of ventricular depolarization Am H art J 51 405
12 SEIDEN G E & R A KEISMAN 1955 The precordial electrocardiogram Is it predominantly derived from the heart muscle immediately beneath the electrode? J Clin Invest 34 962
13 SEIDEN G E 1955 Anatomic location of the electric heart center in patients Circulation 12 773
14 LANGNER P H JR & S R MOORE 1956 Location of the electrical center of ventricular repolarization Am Heart J 52 335
15 WILSON F N & R H BAYLEY 1950 The electric field of an eccentric d pole in a homogeneous spherical conducting medium Circulation 1 84
16 FRANK E 1952 Electric potential produced by two point current sources in a homogeneous conducting sphere J Appl Phys 23 1225

17 Frank E 1953 Theoretic analysis of the influence of heart-dipole eccentricity on limb leads Wilson central terminal voltage and the frontal plane vectorcardiogram Circulation Research 1 380
18 Yeh G C K J Martinek & C S S Ludford 1955 The potentials due to certain singularities in the presence of a fixed sphere J Soc Industr Appl Math 3 142
19 Frank E 1955 Determination of the electrical center of ventricular depolarization in the human heart Am Heart J 49 670
20 Okada R H 1956 Potentials produced by eccentric current dipole in a finite length circular conducting cylinder Submitted for publication
21 Burger H C H A Tolhoek & F G Backbier 1954 The potential distribution on the body surface caused by a heart vector Am Heart J 48 249
22 Frank E 1953 The zero-potential contour on a homogeneous conducting cylinder IRE Trans on Med Electronics 1 27
23 Wait J R 1953 The potential of two current point sources in a homogeneous conducting prolate spheroid J Appl Phys 24 496
24 Schmitt O H & R B Levine 1951 Determination of vector-electrocardiographic structure constants of the human body through use of plastic replicas Am J Physiol 167 824
25 Frank E & C F Kay 1953 A reference potential for unipolar electrocardiographic measurements on models Am Heart J 46 195
26 Frank E 1956 Analysis of R L F B systems of spatial vectorcardiography Am Heart J 51 34
27 Frank E & C F Kay 1954 Frontal plane studies of homogeneous torso models Circulation 9 724
28 Okada R H 1956 The image surface of a circular cylinder Am Heart J 51 489
29 Frank E 1954 The image surface of a homogeneous torso Am Heart J 47 757
30 Frank E 1955 Absolute quantitative comparison of instantaneous QRS equipotentials on a normal subject with dipole potentials on a homogeneous torso model Circulation Research 3 243
31 Frank E 1954 A direct experimental study of three systems of spatial vectorcardiography Circulation 10 101
32 Frank E C F Kay G E Seiden & R A Keisman 1955 A new quantitative basis for electrocardiographic theory the normal QRS complex Circulation 12 406
33 Schmitt O H & E Simonson 1955 The present status of vectorcardiography Arch Internal Med 96 574
34a McFee R & F D Johnston 1953 Electrocardiographic leads I Introduction Circulation 8 554
34b McFee R & F D Johnston 1954 Electrocardiographic leads II Analysis Circulation 9 255
34c McFee R & F D Johnston 1954 Electrocardiographic leads III Synthesis Circulation 9 868
35 Brody D A & W E Romans 1953 A model which demonstrates the quantitative relationship between the electromotive forces of the heart and the extremity lead Am Heart J 45 263
36 Frank E 1956 An accurate clinically practical system for spatial vectorcardiography Circulation 13 737
37 Frank E & G E Seiden 1956 Comparison of limb and precordial vectorcardiographic systems Circulation 14 83
38 Hirsch J I S A Briller & N Marchand 1955 The image tetrahedron in man determined by reciprocal stimulation of a tri dimensional esophageal electrode Circulation 12 723
39 Brody D A B D Erb & W E Romans 1956 The approximate determination of lead vectors and the Burger triangle in normal human subjects Am Heart J 51 211
40 Frank E 1956 Planar dipole loops Circulation Research 4 257

THE POTENTIAL OF A GENERAL DIPOLE IN A HOMOGENEOUS CONDUCTING PROLATE SPHEROID*

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The purpose of this paper is to present the potential expression of a general dipole in a homogeneous conducting prolate spheroid that will prove useful in the theoretical aspects of electrocardiography.

A prolate spheroidal body of homogeneous conductivity has a semimajor axis a and semiminor axis $a\sqrt{1-e^2}$, where $0 \leqslant e \leqslant 1$ is the eccentricity. The equation of its surface is given by

$$\frac{\rho^2}{1-e^2} + z^2 = a^2 \tag{1}$$

where a conventional cylindrical coordinate system (z, ρ, θ) is chosen so that the spheroid is coaxial with the z axis. A dipole of strength μ and direction along the unit vector $\overline{B}$ is located at (z_0, ρ_0, θ_0) inside the spheroid.

It is now convenient to introduce the prolate spheroidal coordinates (ξ, η, φ) in such a way that the following relations exist

$$z = ae\xi\eta$$
$$\rho = ae[(1-\eta^2)(\xi^2-1)]^{\frac{1}{2}} \tag{2}$$

with $1 \leqslant \xi \leqslant \infty$, $-1 \leqslant \eta \leqslant 1$ and $0 \leqslant \varphi \leqslant 2\pi$. The radial coordinate ξ specifies a family of spheroids given by

$$\frac{\rho^2}{(\xi^2-1)} + \frac{z^2}{\xi^2} = a^2e^2 \tag{3}$$

and the angular coordinate η specifies a family of hyperboloids given by

$$\frac{\rho^2}{-(1-\eta^2)} + \frac{z^2}{\eta^2} = a^2e^2 \tag{4}$$

It can be noticed that the spheroids, EQUATIONS 1 and 3, and the hyperboloids, EQUATION 4, are confocal.

In this coordinate system, the surface of the prolate spheroidal body is specified by $\xi = \xi_1$, and the dipole is located at (ξ_0, η_0, φ_0).

From the definition of directional derivative, the potential of the general dipole in an infinite domain can be written in terms of the potential of a unit source ϕ, as follows:

$$\phi_0 = \mu(\overline{B}\cdot\nabla)_{\substack{\xi=\xi_0\\ \eta=\eta_0\\ \varphi=\varphi_0}}\phi = \mu\left(\frac{B_\xi}{h_{\xi_0}}\frac{\partial}{\partial\xi} + \frac{B_\eta}{h_{\eta_0}}\frac{\partial}{\partial\eta} + \frac{B_\varphi}{h_{\varphi_0}}\frac{\partial}{\partial\varphi_0}\right)\phi \tag{5}$$

* This investigation was supported by Research Grant H 2263 from the National Heart Institute of the National Institutes of Health, Public Health Service, Department of Health, Education and Welfare, Bethesda, Md.

where

$$h_\xi = ae\sqrt{\frac{\xi_0^2 - \eta_0^2}{\xi_0^2 - 1}} \qquad h_\eta = ae\sqrt{\frac{\xi_0^2 - \eta_0}{1 - \eta_0^2}}$$
$$h_{\varphi_0} = ae\sqrt{(\xi_0^2 - 1)(1 - \eta_0^2)} \tag{6}$$

and

$$B_{\eta_0}^2 + B_{\xi_0}^2 + B_{\varphi_0} = 1$$

Since (for example Morse and Feshbach,[1] p 1291)

$$\phi = \frac{1}{R} = \sum_{n=0}^{\infty}\sum_{m=0} \left.\begin{matrix} A_m \\ B_m \end{matrix}\right\} \cos m(\varphi - \varphi_0) P_n^m(\eta) \begin{cases} Q_n^m(\xi) & \text{for } \xi > \xi_0 \\ P_n^m(\xi) & \xi < \xi_0 \end{cases} \tag{7}$$

where

$$\left.\begin{matrix} A_m \\ B_m \end{matrix}\right\} = \frac{1}{ae}(2n + 1)\epsilon_m i^m \left[\frac{(n - m)!}{(n + m)!}\right] P_n^m(\eta_0) \begin{cases} P_n^m(\xi_0) \\ Q_n^m(\xi_0) \end{cases} \tag{8}$$

and

$$\epsilon_m = \text{Neumann factor} \begin{cases} = 1 \text{ for } m = 0 \\ = 2 \text{ for } m \neq 0 \end{cases} \tag{9}$$

EQUATION 5 becomes

$$\phi_0 = \sum_{n=0}^{\infty}\sum_{m=0} \begin{matrix} [A_m' \cos m(\varphi - \varphi_0) + A_m'' \sin m(\varphi - \varphi_0)] P_n^m(\eta) Q_n^m(\xi) \\ [B_m' \cos m(\varphi - \varphi_0) + B_m'' \sin m(\varphi - \varphi_0)] P_n^m(\eta) P_n^m(\xi) \end{matrix} \quad \text{for} \begin{cases} \xi > \xi_0 \\ \xi < \xi_0 \end{cases} \tag{10}$$

where

$$\left.\begin{matrix} A_m' \\ B_m' \end{matrix}\right\} = \frac{\mu}{ae}(2n + 1)\epsilon_m i^m \left[\frac{(n - m)!}{(n + m)!}\right]^2 \begin{cases} \left[\frac{B_\xi}{h_{\xi_0}} P_n^m(\eta_0) P_n^m(\xi_0) + \frac{B_{\eta_0}}{h_{\eta_0}} P_n^m(\eta_0) P_n^m(\xi_0)\right] \\ \left[\frac{B_\xi}{h_{\xi_0}} P_n^m(\eta_0) Q_n^m(\xi_0) + \frac{B_\eta}{h_{\eta_0}} P_n^m(\eta_0) Q_n^m(\xi_0)\right] \end{cases} \tag{11}$$

and

$$\left.\begin{matrix} A_m'' \\ B_m'' \end{matrix}\right\} = \frac{\mu}{ae}\frac{B_\varphi}{h_{\varphi_0}}(2n + 1) m \epsilon_m i^m \left[\frac{(n - m)!}{(n + m)!}\right]^2 P_n^m(\eta_0) \begin{cases} P_n^m(\xi_0) \\ Q_n^m(\xi_0) \end{cases} \tag{12}$$

The disturbance potential ϕ_1 due to the presence of a prolate spheroid $\xi = \xi_1$ is a solution of the Laplace equation and can be represented in terms of spheroidal harmonics as follows

$$\phi_1 = \sum_{n=0}^{\infty} \sum_{m=0}^{n} [C_{mn} \cos m(\varphi - \varphi_0) + D_{mn} \sin m(\varphi - \varphi_0)] P_n^m(\eta) P_n^m(\xi) \quad (13)$$

where C_{mn} and D_{mn} should be chosen in such a way that the normal flow or the normal derivative of the total potential $\phi = \phi_0 + \phi_1$ will be zero at the body surface $\xi = \xi_1$. This gives rise to the following relation

$$\phi_0'(\xi_1) + \phi_1'(\xi_1) = 0 \quad (14)$$

where the prime indicates a differentiation with respect to ξ. Since $\xi_1 > \xi_0$ we have from EQUATIONS 10, 13 and 14

$$\left. \begin{matrix} C_{mn} \\ D_{mn} \end{matrix} \right\} = -\frac{Q_n^{m\prime}(\xi_1)}{P_n^{m\prime}(\xi_1)} \begin{cases} A_{mn}' \\ A_{mn}'' \end{cases} \quad (15)$$

$(C_{00} = D_{00} = 0$ since $A_{00}' = A_{00}'' = 0)$

The total potential ϕ at (ξ, η, φ) in the spheroidal body due to the general dipole is then explicitly given by

$$\phi = \phi_0 + \phi_1$$

$$\begin{cases} = \displaystyle\sum_{n=1}^{\infty} \sum_{m=0}^{n} [A_{mn}' \cos m(\varphi - \varphi_0) + A_{mn}'' \sin m(\varphi - \varphi_0)] \\ \qquad \left[Q_n^m(\xi) - \dfrac{Q_n^{m\prime}(\xi_1)}{P_n^{m\prime}(\xi_1)} P_n^m(\xi)\right] P_n^m(\eta) \qquad \text{for} \quad \xi_1 \geqslant \xi > \xi_0 \\ = \displaystyle\sum_{n=1}^{\infty} \sum_{m=0}^{n} \left[\left\{B_{mn}' - \dfrac{Q_n^{m\prime}(\xi_1)}{P_n^{m\prime}(\xi_1)} A_{mn}'\right\} \cos m(\varphi - \varphi_0)\right. \\ \qquad \left. + \left\{B_{mn}'' - \dfrac{Q_n^{m\prime}(\xi_1)}{P_n^{m\prime}(\xi_1)} A_{mn}''\right\} \sin m(\varphi - \varphi_0)\right] P_n^m(\xi) P_n^m(\eta) \\ \qquad\qquad + B_{00} \qquad \text{for} \quad \xi < \xi_0 \end{cases} \quad (16)$$

where A_{mn}', A_{mn}'', B_{mn}' and B_{mn}'' are given by EQUATIONS 11 and 12.

On the body surface $\xi = \xi_1$ the potential at (ξ_1, η, φ) reads

$$\phi(\xi_1) = \phi_0(\xi_1) + \phi_1(\xi_1) = \sum_{n=1}^{\infty} \sum_{m=0}^{n} [A_{mn}' \cos m(\varphi - \varphi_0)$$
$$+ A_{mn}'' \sin m(\varphi - \varphi_0)] \left[Q_n^m(\xi_1) - \frac{Q_n^{m\prime}(\xi_1)}{P_n^{m\prime}(\xi_1)} P_n^m(\xi_1)\right] P_n^m(\eta) \quad (17)$$

The associated Legendre functions in these expressions are extensively tabulated (for example Hobsen and Jahnke and Emde[3]) so that the numerical values for any interesting cases are computable. In connection with wake and

thrust deduction in shipbuilding,[4] we have treated a special case of the potential of a radial dipole outside a prolate spheroidal rigid body The potential expression for a general dipole in an oblate spheroidal body can be obtained in a similar manner

References

1 Morse P M & H Feshbach 1953 Methods of Theoretical Physics McGraw Hill New York N Y
2 Hobsen F W 1931 Spherical and Ellipsoidal Harmonics Cambridge Univ Press Cambridge England
3 Jahnke F & F Emde 1945 Tables of Functions Dover Publications New York N Y
4 Martinek J & G C K Yeh 1955 Theoretical Studies of Wake and Thrust Deduction (a Contribution to Potential Theory in Three Dimensions) Final Rept No II Reed Research Inc Washington D C

THE CONDUCTIVITY OF LIVING TISSUES*

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Studies of the potential distribution on the surface of the human body have shown that the electrical activity of the heart can be represented by a fixed location rotating dipole of time dependent magnitude as summarized in Frank s preceding paper The location of this dipole can be expected to coin cide in space only with the electrical center of the heart when variation of re sistivity of the tissues surrounding the heart is small Therefore investigation of the homogeneity of the electrical properties of tissue is indicated Further more it is desirable to determine whether the capacitance of tissue components is sufficiently small throughout the cardiac frequency spectrum to justify neg lect of capacitive current components in any theory of the ECG If the capac itance of tissue were found to be excessive, the electrical phase angle of the transfer impedance which is defined by heart dipole current and surface body potential would be sufficiently large and variable with frequency to affect the shape of the ECG In this case surface potentials would depend not only on heart activity and purely geometrical factors but also on electrical impedances of the various tissue complexes involved These facts aside from our general interest in tissue impedance stimulated our investigations of tissue impedance *in situ* at low frequencies

We have discussed our data and associated technical problems in detail previously[1–4] We shall therefore summarize here the results only to an extent sufficient to answer the questions formulated above We restrict ourselves to values measured *in situ* in living dogs with current levels that are small enough to avoid excitation that is we report data that characterize the passive elec trical characteristics of tissue as existent for the currents generated by the heart The frequency dependence of the resistivity of liver is demonstrated in FIGURE 1 The curve is characteristic for all samples of muscular liver and lung tissue while the frequency dependence of fatty tissue shown also in the figure is somewhat smoother TABLE 1 gives the specific resistance data of various tissues averaging hundreds of values at 10 100 and 1000 cps The data show that the resistances of the major types of tissue surrounding the heart are nearly identical Lung tissue has a value that is perhaps about 20 per cent higher than muscle liver and heart muscle This is not necessarily significant however in view of comparable standard deviation values that characterize variation from one sample to another[4] The resistance values are higher than those previously stated by others[5, 6] They agree much better with theoretical expectation which is based on the amount of cellular volume concentration and air and blood content in areas such as the lung[5] An excep- tion is fatty material whose resistivity is substantially larger than that of

*This investigation was supported in part by Research Grants H 339 and H 1253(C2) from the National Institutes of Health Public Health Service Department of Health Education and Welfare Bethesda Md

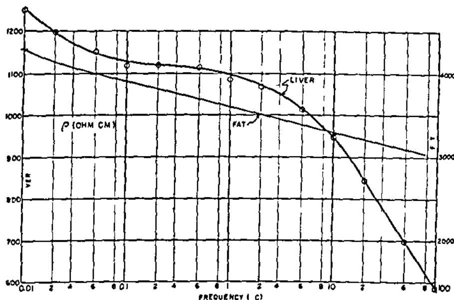


FIGURE 1 Specific resistance of liver and fat tissue *in situ* as a function of frequency The frequency dependence is characteristic for all tissues that have been investigated with the exception of fatty tissue

TABLE 1

SPECIFIC RESISTANCE OF VARIOUS BODY TISSUES IN *SITU* AT 10 100 1000 AND 10 000 CPS

ρ ohm cm	10 cps	100 cps	1000 cps	10 000 cps
Lung	1120	1090	1040	950
Muscle	965	880	830	760
Liver	840	800	765	685
Heart muscle	965	925	845	600
Fatty tissue			1500–5000	

The values in this and the following tables are averages of about 20 single observations in each case The standard deviation which characterizes variations from sample to sample at each frequency and type of tissue is about 25 per cent No significant difference exists therefore between lung muscle liver and heart muscle averages Change with frequency can be stated as accurately as the measurements were obtained (1 to 2 per cent)

other tissues due to its lower electrolyte content This should not affect the potential distribution on the body surface noticeably however at least not as long as the fat deposit is restricted to a layer of subcutaneous material whose thickness is very small compared with the trunk dimensions

Not included in our material are the values that characterize bone structures Measurements carried out at much higher frequencies show that bone resistivity is high This and the fact that resistivity can increase only with a decrease in frequency establishes bone structures as insulating at least by comparison with other tissues Here again we may guess that bone should not affect the potential distribution on the body surface seriously in view of the small volume and cross section of the bone structures surrounding the heart Two dimensional experiments by others support the validity of this argument [7]

TABLE 2

AVERAGES OF THE DIELECTRIC CONSTANT GIVEN IN MULTIPLES OF 1000 FOR VARIOUS FREQUENCIES AND BODY TISSUES

$\times 10^{-3}$	10 cps	100 cps	1000 cps	10 000 cps
Lung	25 000	450	85	25
Muscle	30 000	800	130	55
Liver	50 000	850	145	55
Heart muscle	20 000	820	320	100
Fatty tissue		150	50	20

The values at 10 cps are likely to be 3 to 10 times smaller than quoted. Standard deviation of the values given in the tables is about 30 per cent. There is no significant difference between lung, muscle, liver and heart muscle values.

The capacitance data reported in detail elsewhere[8] are summarized in TABLE 2 and expressed in terms of dielectric constants, that is, values that are 3.6 π times larger than the capacitance of a cubic centimeter tissue expressed in $\mu\mu$ farads. The data are averages and they are given for various frequencies and are seen to depend strongly on frequency. The products $R\omega C$ characterize the ratio of capacitive to resistive current; they are given in TABLE 3 and are obtained from resistance R and capacitance C. They show that the capacitive contribution to the total current is very small even though the dielectric constant values are very large. We conclude, therefore, that the tissues surrounding the heart establish not only a reasonably homogeneous but, for all practical purposes of present electrocrdiographic theory, a purely resistive medium.

A large uncertainty in the capacitance (TABLE 2) and the ratio of capacitive to resistive current (TABLE 3) at 10 cps has its origin in the substantial amount of electrode polarization that occurs at the interface of the electrode system and the surrounding tissue. This uncertainty could be reduced only with much larger electrode arrangements than are practical for *in situ* work. A careful analysis of the polarization of our system has been conducted[4, 8] and, as a consequence, the upper limit statements in TABLES 2 and 3 can be made. The values given for 10 cps are quite conservative, that is, indications are that

TABLE 3

AVERAGES OF THE RATIO OF CAPACITIVE TO RESISTIVE CURRENT FOR VARIOUS FREQUENCIES AND BODY TISSUES

$R\omega C$	10 cps	100 cps	1000 cps	10 000 cps
Lung	0.15	0.0[illegible]5	0.05	0.14
Muscle	0.15	0.035	0.06	0.24
Liver	0.20	0.035	0.06	0.20
Heart muscle	0.10	0.04	0.15	0.32
Fatty tissue		0.01	0.03	0.15

The values at 10 cps are possibly 3 to 10 times smaller than quoted. The values demonstrate that only to a first approximation do body tissues show resistive character. If dielectric constants were another order of magnitude higher than shown in TABLE 2, large ratios of capacitive to resistive current would result. The standard deviation is about 30 per cent.

capacitance values are lower than the upper limits quoted in TABLE 2 There is no need to be less conservative since even the upper limits quoted in TABLE 2 yield values for the ratio of capacitive to resistive current which again demonstrates the resistive character of the current If observed dielectric constants were tenfold higher than reported here appreciable ratios of capacitive to resistive current would exist and major complications in electrocardiographic theory would appear *It is fortunate that nature while providing dielectric* constants in the million range limited itself enough to make electrocardiography possible

The results presented in TABLES 1 2 and 3 and FIGURE 1 extend down to only 10 cps while the frequency spectrum characteristic for the electrical heart activity extends to 1 cps Therefore it is necessary to justify the applicability of our data to the total frequency spectrum of interest FIGURE 2 summarizes the frequency dependence of the dielectric constant of muscular tissue over the total range of frequency that can be covered with presently available techniques with excised tissue samples It demonstrates that the changes with frequency occur in three major steps, which we call the α β and γ dispersion In electrocardiography we are concerned only with α and β dispersion since frequencies in excess of 1 or 10 kc are not represented in the ECG The mechanism responsible for the β dispersion is understood quite well thanks to the fundamental work of various investigators especially K S Cole H J Curtis and H Fricke The effect in the β region is caused by an electrical time constant that is determined by the capacitance of the individual cell envelope and the resistivity of the cell interior This introduction of the concept of a time

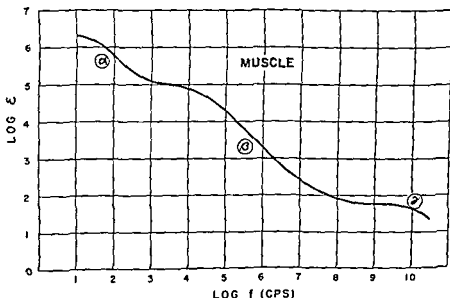


FIGURE 2 Frequency dependence of the dielectric constant of muscular tissue showing three different regions of marked frequency dependence

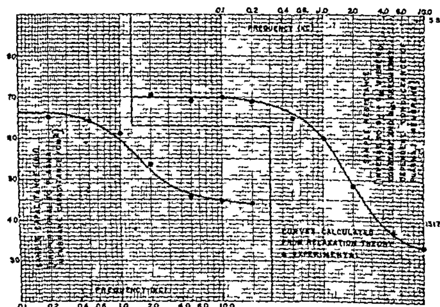


FIGURE 3. Low frequency dependence of capacitance and resistance of a sample of erythrocytes. The dependence is characteristic of a corresponding frequency dependence of the plasma membranes properties. The agreement between the experiment and the simple relaxation theory demonstrates that the existence of one time constant is responsible for the observed effects. The erythrocytes are hemolyzed osmotically and measured at room temperature.

constant which reflects the biological microstructure had been further refined by association with the membrane properties typical for polarizable interfaces. Another approach assumes the existence of a spectrum of electrical time constants reflecting the statistical irregularity of the microstrcture of tissue.

The α change is of major concern to us since the understanding of its effect is intimately associated with the extrapolation of our measurements down to 1 cps. It reflects changes in the cell membrane's electrical properties. This follows from the fact that the capacitance which is measured at low frequencies (<1 kc for tissue) has been proven to be in direct proportion to the capacitance of the cell membranes. The conductance is the sum of a frequency independent value characteristic of the cell environment and a second smaller part that is frequency dependent and characteristic of the cell membrane's permeability. We have been able to obtain α curves of great analytical simplicity as demonstrated in FIGURE 3 for a suspension of hemolyzed erythrocytes. Here the cell membranes of the erythrocyte behave in exact agreement with a theoretical prediction based solely on two assumptions: (1) linear properties and (2) the existence of only one time constant characteristic of an exponential time dependence of membrane polarization when a step function potential is applied. The assumption of linearity has been checked in all of our experiments and is justified for the biological medium when current density

is kept safely below the excitation level. The existence of only one electrical time constant T so clearly demonstrated in the case of hemolyzed blood cells and characteristic of the cell envelope permits one to relate the frequency dependence of capacitance with the frequency dependence of resistivity as follows:[9]

$$\frac{\Delta C}{\Delta R} = \frac{T}{R}$$

where ΔR and ΔC characterize the change of resistance (in ohms) and capacitance (in farads) as frequency is varied. The equation states that for large time constants as existent in the range of the α dispersion rather large changes in capacitance must correspond to comparatively small changes in resistivity.

FIGURE 4 shows the resistance and capacitance of a piece of excised muscular tissue. Here the α dispersion is very pronounced in capacitance reflecting the fact that its time constant is about 20 times larger than in the case demonstrated in FIGURE 3 while the change in cell membrane conductance can be shown to be comparable to the one occurring in the plasma membrane of the hemolyzed erythrocyte. In both cases shown in FIGURES 3 and 4 we find applicable the theory that relates resistance and capacitance change. In the case shown in FIGURE 4 however the α dispersion runs somewhat flatter than expected on the basis of only one time constant indicating several time constants centered

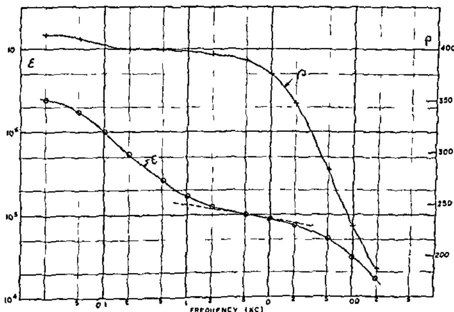


FIGURE 4. Dielectric constant and resistance of a sample of excised muscular tissue shown to demonstrate the small dependence of resistance and the large dependence of dielectric constant upon a frequency below 1 kc. The absolute value of the resistance is somewhat lower than normal. This is caused by a highly conducting Ringer's solution used to establish contact between the sample and the electrodes.

around 1 msec In all measurements with excised material where we have been able to measure capacitance values down to 10 cps and in some cases down to 5 cps we find that resistance values change only slightly below 1 kc and are properly related to observed capacitance change [8] All of our *in situ* measurements which are more difficult to make with precision and permit us to measure only capacitance uninfluenced by electrode polarization down to 100 cps support the observations in excised material Therefore we feel confident that no mechanism other than the above described α dispersion need be considered in a discussion of the dielectric properties of tissue at low frequencies The measured small change in resistivity below 1 kc and the experimentally gained knowledge that the α dispersion is centered above 10 cps permit with the help of the equation given above the prediction of optimal capacitance values below 10 cps This prediction gives values that are too small to establish noticeable capacitive currents or to be of importance in electrocardiography

Conclusions

The resistance values that we measured at 10 cps are almost identical with those found at lower and higher frequencies of interest in electrocardiography Capacitive influences can be neglected in present day electrocardiographic theory and the validity of the assumption of a homogeneous resistive medium around the heart is justified to a first approximation The only exception in this picture is the heart itself Heart muscle of a resistivity of about 1000 ohm cm surrounds blood of a resistivity of only 100 ohm cm Therefore the total heart complex establishes in itself an enormously inhomogeneous and in its inhomogeneity rhythmically changing complex The tremendously low conductivity of the blood in the heart chamber may well contribute to the understanding of the fixed location dipole behavior of the heart

References

1 SCHWAN H P C F KAY & T P BOTHWELL 1954 Electrical resistivity of living body tissues at low frequencies Proc Fed Biol Soc 13(1)

2 SCHWAN H P C F KAY T P BOTHWELL & F L FOLTZ 1954 Electrical resistivity and capacity of living body tissues at heart signal frequencies Second World Congr Cardiol Washington D C

3 SCHWAN H P 1955 Electrical properties of body tissues and impedance plethysmograph IRE Trans on Med Electronics ME 3 32–46

4 SCHWAN H P & C F KAY 1956 Electrical conductivity of living body tissues as it pertains to electrocardiography II Resistivity of living tissues Circulation Research 4 664

5 BURGER H C & J B VAN MILAAN 1943 Measurements of specific resistance of the human body to direct current Acta Med Scand 114 584

6 FAHRMAN W & F D JOHNSTON 1943 The electrical conductivity of the tissues near the heart and its bearing on the distribution of cardiac action currents Am Heart J 26 42

7 GABOR D & C V NELSON 1954 Determination of the resultant dipole of the heart from measurements on the body surface J Appl Phys 25 413

8 SCHWAN H P & C F KAY 1957 Electrical conductivity of living tissues as it pertains to electrocardiography III Capacitance of living tissues Circulation Research In press

9 SCHWAN H P 1954 Electrical properties of muscular tissue at low frequencies Z Naturforsch 9b 245

the spatial dipole angle) A similar correspondence exists between two- and three-dimensional boundary distributions with other horizontal dipole angles It is therefore possible to draw the following conclusion

If the vertical angle α of a dipole in a cylindrical volume conductor is not greater than about ±30° the distribution of potential around the boundary of the cylinder at the level of the dipole center will be similar in shape for the same horizontal dipole angles to the potential distribution around the boundary of a two-dimensional conductor having the shape of a cross section through the cylinder

It follows from this that two-dimensional measurements can be used to obtain information about the horizontal component of the spatial vector FIGURE 4 gives further evidence of this These charts show the distribution of po-

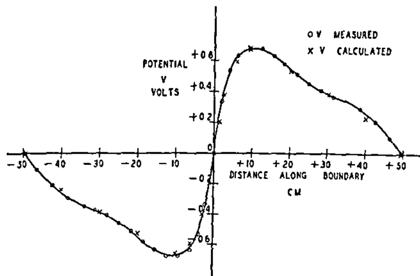


FIGURE 2 Potential distribution around the boundary of a homogeneous thorax cross section The dipole angle is 0 The calculated values are according to EQUATION 12

tential around the periphery of the deep tank at the level of the dipole center for horizontal angles (β) of 0° 30 60 and 90 and for a vertical angle (α) of 0° Comparison with FIGURES 5 and 6 for the same horizontal angles in the two-dimensional thorax section shows that the shapes of the potential distribution curves in the two cases are very similar

Effect of Electrical Inhomogeneity on the Potential Field

The nature of the distortions of the electrical field caused by a finite boundary and by the introduction of good and poor conductors was shown in the model studies of Katz[7] and discussed by Lepeschkin[8] The effect of inhomogeneous areas can best be shown by a comparison with the field of the dipole in a homogeneous medium The charts of FIGURE 5 are all for a β angle of 90 (in this paper positive angles are taken counterclockwise in accordance with long established mathematical conventions) In FIGURE 5a the section is homo-

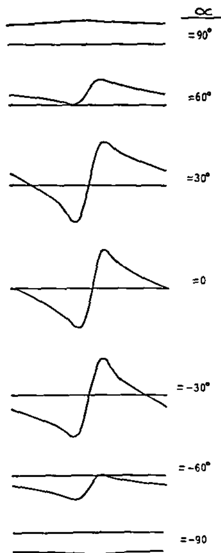


FIGURE 3 Potential distribution around the boundary of a deep tank at the level of the dipole The horizontal angle is 0° and the vertical angle is +90 to −90 at 30° intervals Compare with FIGURE 2

geneous and the departure of the field distribution from that of a dipole in an infinite medium is due solely to the effect of the boundary The curves shown are the equipotentials with values as marked The curves on the right show the variation of potential around the boundary as before The broken curve show the potential gradient along the boundary This is defined as

$$\bar{E} = \frac{dV}{dL} \cong \frac{\Delta V}{\Delta L}$$

$\frac{dV}{dL}$ signifying the derivative of potential with respect to distance along the boundary L and being equal to the slope of the curve of V against L. In practice $\bar{E}$ was computed by taking the ratio of small increments of V and L and ΔV and ΔL. $\bar{E}$ could also be found by moving a pair of closely spaced electrodes around the boundary but this would be no more accurate than calculating $\frac{\Delta V}{\Delta L}$. Since $i = k\bar{E}$ where i is the current intensity vector and k is

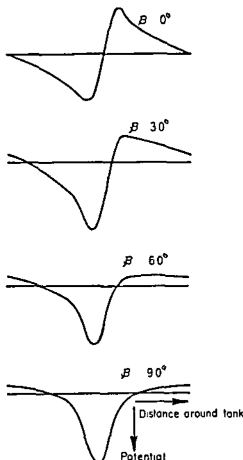


FIGURE 4. Potential distribution around the boundary of a deep tank at the level of the dipole. The vertical angle is 0, the horizontal angle 0, 30, 60, and 90. Compare with FIGURES 5 and 6.

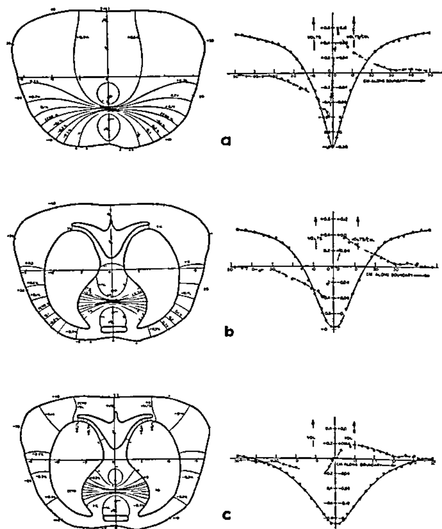


FIGURE 5 Field and boundary potential distributions in a 2 dimensional thorax section for a β angle of 90 Figure *a* shows the homogeneous section in *b* the spine and sternum sections are completely insulating and the lungs have a resistivity ratio of 4 and in *c* the lung sections are also completely insulating The broken curves in the right hand illustrations show the distribution of potential gradient around the boundary

the conductivity the potential gradient curves also are proportional to the variation of current intensity along the boundary As is obvious from FIGURE 5a E is greatest near the center of the front of the section

FIGURE 5b shows the field when insulating spine and sternum sections and lung sections with a resistivity four times as great as that of the main body of

the electrolyte have been added This is the value of relative lung resistivity found by Burger and van Milaan [9] In this case the internal field is not greatly altered although the 1 v equipotentials are changed The shape of the boundary potential distribution curve is similar to that of the homogeneous section except that the maximum negative potential is now −0 77 v instead of −1 v This potential reduction may be due to a shielding action of the sternum which is directly in line with the dipole axis Also, the potential gradient peaks are lower in amplitude and more widely separated from each other In FIGURE 5c the lung sternum and spine sections are completely insulating These conditions were also tried on the basis of the experiments of Lindner and Katz [10] in which it was concluded that the lungs are completely insulating Also if completely insulating lung models did not have too much effect then lower values of resistivity would be unimportant In this case however the internal field is considerably altered The +1 v equipotential is altered in shape and the zero-potential line is shifted toward the back The potential distribution between the lung and spine sections is completely different The boundary potential distribution curve is similar in its general shape to the curves of FIGURES 5a and 5b but the potentials are negative over nearly the entire boundary It might be argued that the changes in boundary potential were due merely to shifts in the voltage of the reference electrode Although the reference probe potential probably did change slightly a comparison of the potential gradient curves which are independent of the reference potential shows that the changes in potential are due mainly to the change in internal conditions In FIGURES 5a to 5c for example the maximum slope values are approximately 0 12 0 08 and 0 04 v /cm Due to conditions of symmetry that exist with β angles of 90° the potential maxima (M) are located at the ends of the extended dipole axis

Potential distributions were also measured for other dipole angles and in each case it was found that there was not a great deal of difference between the cases *a* and *b* that is between the homogeneous section and the section using lungs with a resistivity ratio of 4 The completely insulating lungs caused a considerable distortion of the field however FIGURE 6 shows the distributions obtained in the sections using dipole angles (β) of 0° 30 and 60 with a lung resistivity ratio of 4 FIGURE 5b with a β angle of 90° can be considered part of this series

As the dipole rotates the field pattern changes markedly The zero potential points remain fairly close to the dipole transverse axis but the points of maximum positive and negative potential (M) do not remain at the ends of the dipole axis As Hess[11] and Schaefer[12] pointed out when the dipole is not at the center of the section the points of maximum potential lie along a curved arc passing through the poles of the dipole It is interesting to note however that a line joining the maxima is roughly parallel to the dipole axis The location of the zero potential points depends upon the reference electrode s being a true null point On the other hand the location of the potential maxima is independent of the reference potential since a change in the reference potential would be added to or subtracted from the potential of every point in the field

FIGURES 6 and 5b also show how the distribution of potential around the

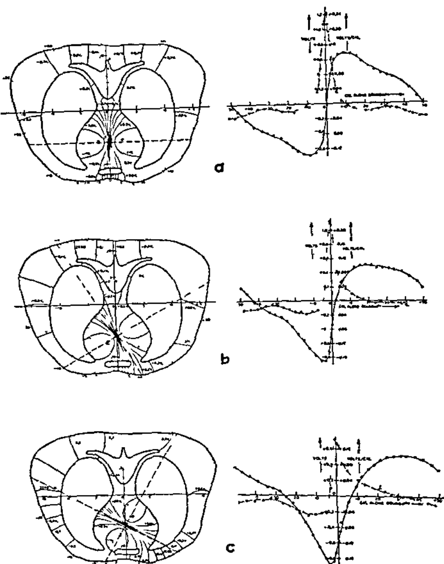


FIGURE 6 Field and boundary potential distributions in a 2-dimensional thorax section for β angles of 0 (*a*) 30 (*b*) and 60 (*c*) In all cases the lungs have a resistivity ratio of 4 and the spine and sternum sections are completely insulating FIGURE 5b forms part of this series for a β angle of 90

boundary changes as the dipole rotates For β angles of 0 30 and 60° the potential gradient is maximum at the point on the boundary nearest to the dipole center (0 cm) This illustrates a possible method of finding the location of the resultant dipole of the heart from measurements on the chest wall

In measurements of the distribution of potential around the chest at the mid ventricular level[13] the peak of the potential gradient curve was usually from 3 to 8 cm to the left of the mid sternal line FIGURE 5b shows however, that if the dipole angle is 90 the potential gradient curve is biphasic, with positive and negative maxima equally spaced about the dipole center In this case the potential gradient at the point on the boundary nearest the dipole center is zero The points of zero gradient coincide with points of maximum or minimum potential since at these points the curve of potential against distance must have zero slope Changes of reference potential would have absolutely no effect on the potential gradient curves and would cause only an upward or downward shift of the entire potential curve

Because of this fact no attempt was made to find an exact zero reference potential The reference electrode was placed either midway between the poles of the dipole or at a remote point of the tank It would have been possible to use the reference potential at the junction point of two resistors[14, 15] but this would have necessitated precautions to avoid any polarization of the current electrodes Frank and Kay[15] have discussed the problems involved with the above two types of reference systems A more elaborate method is that of Sugi[16] who put three electrolytic tanks in series by means of wicks and put his reference electrode in a neutral tank Experiments are now in progress in this laboratory to adapt the double layer tank[2] to measurements in which a finite boundary is present in the upper layer The technique is to leave a very narrow gap in the boundary and to use the bottom layer electrode as the reference point The gap should have a negligible effect on the potential distribution inside the boundary

The effect of increasing the resistivity of the lung sections was also studied for other dipole angles The results are given in TABLE 1

Dipole 0° The only significant changes between the homogeneous section and the section in which the lung areas had a resistivity ratio of 4 was that the maximum potential gradient increased by 12 per cent and the potential maxima on the boundary shifts in location by about 1 cm When the ratio increased from 4 to infinity the magnitudes of both positive and negative potential maxima decreased and the lateral wall potentials also decreased The potential maxima were located much nearer the front of the section These effects may be explained by the increased shielding action of the lung sections

Dipole 30 As the resistivity ratio was changed from 1 to infinity the magnitude of the maximum negative potential on the right side increased but the maximum positive potential on the left side fell The side wall potentials varied in the same way The left side maximum potential dropped to about one third of its original value whereas the increase in right side maximum potential was only 13 per cent The locations of the potential maxima and zero points on the boundary did not change to any great extent The maximum potential gradient increased in value as the resistivity ratio increased from 1 to 4 and then decreased again as the ratio increased from 4 to infinity As the resistivity of the lung sections increased the right lung tended to channel the current toward the front of the thorax and this caused the potential in this region to increase At the same time, however the left lung impeded the flow

TABLE 1

EFFECT OF CHANGES IN RELATIVE RESISTIVITY OF LUNG SECTIONS

1	2	3		4		5		6	7	8	
β	Res ratio	V_{max} magnitude volts		V_{max} location cm		V_{min} location cm		E_M magnitude volts/cm	E_M location cm	V lateral wall volts	
		R	L	R	L	R	L			R −25 cm	L +25 cm
0	1	− 68	68	−10 2	10 4	0	49 5	214	0	− 45	45
	4	− 69	68	−9 2	9 2	0	49 5	244	+0 5	− 46	46
	∞	− 60	54	−5 8	5 8	− 0 1	49 5	250	0	− 30	24
30	1	− 77	60	−5	18 4	−40 1	2 5	196	+0 5	− 22	57
	4	− 86	51	−4	18 4	−42 4	2 1	223	−0 4	− 29	49
	∞	− 89	21	−4	17	−48	2 6	20	0	− 33	20
60	1	− 87	53	−2	31	−22 8	6 8	150	+1 1	06	52
	4	− 88	51	−4	32	−25 6	7	142	−0 4	− 02	49
	∞	−1 03	09	−3 6	40	−47	23	132	+0 4	− 30	03
90	1	−1	52	0 2	49 5	−13 6	14 1	± 115	±2 6	34	34
	4	− 77	47	0	49 5	−15 2	15 3	± 075	±5 2	31	31
	∞	− 88	03	0	49 5	−42	42	± 040	±5	− 20	20

Column 1 is the dipole angle Column 2 shows the resistivity ratio of the lung sections (resistivity ratio 1 is the homogeneous section and for ratios of 4 and infinity the insulating spine and sternum sections were also in the tank) Columns 3 and 4 give the magnitude and location of points of maximum positive and negative potential on the thorax boundary Column 5 shows the location of the points of zero potential Columns 6 and 7 show the magnitude and location of the peak of the potential gradient curve on the boundary Column 8 gives the potential at points on the right and left lateral walls of the thorax section at distances from the mid sternal line of −25 cm and +25 cm

of current to the left side of the thorax and the potential in this region was decreased

Dipole 60 Again with increasing lung resistivity ratio the magnitude of the maximum negative potential on the right side was increased and the maximum positive potential on the left side decreased The location of the potential maxima and the zero points showed a marked change The maximum potential gradient showed a steady decrease and the side wall potentials were considerably altered The shape of the potential gradient curve also changed At +6 cm on the boundary for example the value of $\overline{E}$ changed from 0 06 v /cm to 0 03 v /cm This means that the slope of the potential curve is smaller and the curve is more spread out as found It is possible however that the increased negativity of the entire curve may be partly due to a change in the reference potential

Dipole 90° The complete set of charts for the dipole at 90° is shown in FIGURE 5 and it has been previously discussed The complicated effect of the inhomogeneous areas can again be emphasized by noting that as the lung resistivity ratio increased the maximum negative potential on the boundary changed from −1 0 v to −0 77 v and back to −0 88 v The fact that the posterior sides and back were not more positive may possibly be due to the shielding action of the spine section

Effect of Greater Conductivity of the Heart Area

In the experiments discussed so far the effect of the relatively greater conductivity of the heart[10, 17, 18] due to the blood has been neglected. In order to test this point the thorax model was rearranged so that the depth of the electrolyte was made greater over the heart area. This was done by merely cutting a piece the shape of the heart cross section (at mid ventricular level) out of the plastic base of the model. The resistivity is best expressed in terms of the resistivity ratio G which is defined as the ratio of the resistivity of an area to that of the main body of the electrolyte. The bottom diagram of FIGURE 7 shows the boundary distributions for the following conditions: dipole β at 90°, G for the heart area 0.45, G for the lung section 4, and G for the spine and sternum section infinite. A comparison of this with the top curve in which the heart area G is 1.0 showed that the boundary distributions are similar in shape but that there is an over all reduction in amplitude with the highly

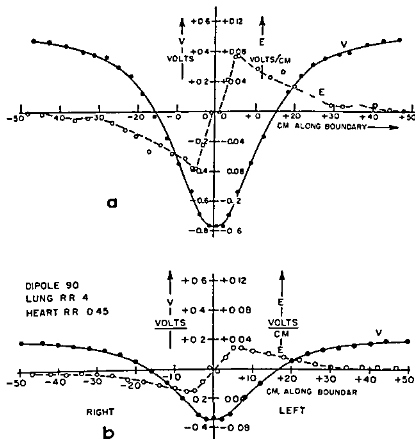


FIGURE 7. Boundary potential distribution for a β angle of 90° with a uniform heart area (a) and with a heart area of increased conductivity (b).

conductive heart area. The positions of the zero points and potential maxima remain unchanged. This is in agreement with physiological experiments in which it was concluded that the effect of the relatively greater conductivity of the heart was uniformly to scale down the electrocardiographic potentials[19] and that increased filling of the frog heart reduced the electrical response.[20] A reduction in external potentials was also observed when good electrical conductors were placed on the ventricle of the dog heart.[21] Such effects have been attributed to the "shunting" action of the blood.[20-22]

Effect of Two Dipoles Acting Simultaneously

Lewis[23] and others have considered that the left and right ventricles may have individual effects on the electrocardiogram, at least in the chest leads. In 1933 Rijlant,[24] using a cathode ray oscilloscope with an amplification of about 3 cm./mv. and a film speed of about 250 mm./sec., found notching not only in the R wave but also in the P and S waves. He attributed his results to the simultaneous recording of two or more activities. In order to study the effect of independent regions of excitation of the heart on chest potentials, experiments were carried out with two separate dipoles in the heart area of the thorax section simultaneously. It was found that if the centers of the two dipoles were located at the same point the boundary potential distribution was identical with that produced by a single dipole that was the vector sum of the two separate dipoles. If the centers of the two dipoles did not coincide, however, the effect of each dipole could be seen. In the experiments of FIGURE 8 two dipoles were located in the ventricular area about 2.5 cm. to the right and left of the mid sternal line. In FIGURE 8a the right ventricular dipole β angle was 0 and the left heart dipole β angle was 22. The only noticeable effect was the dip in the potential gradient curve. In FIGURE 8b the values of β were 90 for the right ventricle and 180° for the left ventricle. Although the potential curve was similar to one that would be obtained from a single dipole, the presence of the extra dipole was indicated by the change in slope of the potential curve and the corresponding dip in the potential gradient. In the model experiments with a single dipole, smooth curves were obtained for the variation of potential and gradient around the boundary. In FIGURE 8c the β angle was 137 for the right ventricle and −130° for the left ventricle. In this case the distributions are complicated and they could not be taken for a single dipole curve. In the three cases shown, the peaks of the potential gradient curves do *not* accurately indicate the locations of the dipoles. This method of finding the dipole location can, therefore, be used only when there is a single effective dipole in action. It is evident that the greater the physical separation between the two dipoles, the greater will be the individual effect of each dipole on the surface potential. These experiments indicate that whereas the vectorcardiogram taken at remote points will give the resultant dipole, chest leads near the heart should also be taken to obtain information about local excitation of the heart. The two types of measurement provide complementary data.

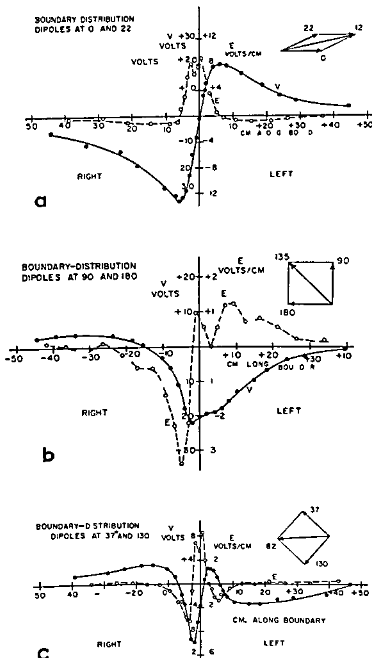


FIGURE 8 Boundary potential distributions with separate dipoles located in right ventricular and left ventricular areas In *a* the β angles are 0 and 22 in *b* 90 and 180 and in *c* 137 and −130 The vector diagrams show the vector that would result if both component vectors were located at the same point A comparison of these curves with those of FIGURE 6 shows the degree of departure from the corresponding resultant d pole

Distributed Source in Thorax Section

It was previously shown[2] that the field of two half shells in an infinite medium was equivalent to a dipole field at remote points When the distributed source was in the thorax section in the heart area the distance between its front surface and the nearest point on the boundary was only 3 cm Even under these conditions however it was found that the boundary potential distribution was very similar to that of the equivalent dipole

*Application of Method of Images to Study of Effects of Regions of High or Low Resistivity**

When the potential of a source in a volume conductor enclosed by an insulating boundary is considered[2] the ratio of resistivities of the media concerned is infinite The method of images can also be used when the resistivity ratio is finite Using the method of calculation of Hague[25] the image system for a current source in the vicinity of a circular disk of finite resistivity has been derived It has been found that four image systems are required depending on whether the current source and sink are inside or outside the disk and whether potentials are required inside or outside the disk

(1) *Source and sink inside disk potentials inside disk* If in the thorax section the heart area is considered circular in shape then this case would be analogous to the case of potentials inside the heart due to the heart electromotive force (E M F) taken as a dipole or point source and sink For this and the other three cases the following symbols are used

V = potential at a point P inside the disk
V = potential at a point P outside the disk
ρ = resistivity of disk
ρ = resistivity of medium surrounding disk
$G = \frac{\rho}{\rho}$ = resistivity ratio
I = current
d = depth of electrolyte (assumed constant)
a = distance from sink to center of disk
b = distance from source to center of disk
r_1 = distance from P to sink
r_2 = distance from P to source
r_3 = distance from P to image of sink
r_4 = distance from P to image of source

$$A = \frac{\rho I}{2\pi d}$$

The sink and source are located at distances a and b from the center of the

* The term image as used here should not be confused with the image surface of Burger and van Milaan[22] – or with mirror image electrocardiograms on the chest wall

disk (FIGURE 9). The images are located along the radii extended at distances from the center $\frac{R}{a}$ and $\frac{R^2}{b}$ where R is the radius of the disk. The potential at a point P inside the disk is then

$$
\begin{aligned}
V &= \frac{\rho GI}{2\pi d}\left[\ln\frac{r_1}{r_2} + \frac{1-G}{1+G}\ln\frac{ar_3}{br_4}\right] \\
&= GA\left[\ln\frac{r_1}{r_2} + \frac{1-G}{1+G}\ln\frac{ar_3}{br_4}\right]
\end{aligned}
\tag{1}
$$

If it is assumed that the average resistivity of the heart is one half that of the surrounding region, then from EQUATION 1

$$V = \frac{A}{2}\left[\ln\frac{r_1}{r_2} + \frac{1}{3}\ln\frac{ar_3}{br_4}\right] \tag{2}$$

The potential of the source and sink in a homogeneous medium of resistivity ρ would be

$$V = A\ln\frac{r_1}{r_2} \tag{3}$$

The lower resistivity in the heart area, therefore, has a complicated effect on the internal potentials.

(2) *Source and sink inside disk—potentials outside disk* (FIGURE 10). In this case there are no images outside the disk, but the original source and sink $+I$

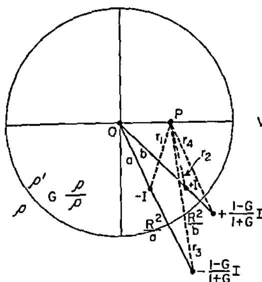


FIGURE 9. Image system for potential at P *inside* the disk due to the source $(+I)$ and sink $(-I)$ *inside* the disk.

and $-I$, are replaced by a source of strength $+\frac{2G}{1+G}(I)$ and a sink of strength $-\frac{2G}{1+G}(I)$ The potential at any external point is then

$$V = \frac{2G}{1+G} A \ln \frac{r_1}{r_2} \tag{4}$$

and for a resistivity ratio of 0 5,

$$V = \frac{2}{3} A \ln \frac{r_1}{r_2}$$

The effect of the lower heart resistivity is therefore, *uniformly* to scale down

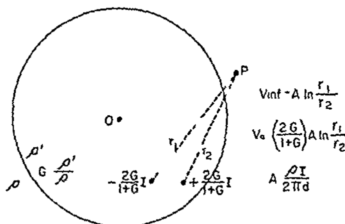


FIGURE 10 Image system for potential at P outside the disk due to the source ($+I$) and sink ($-I$) inside the disk

all external potentials This agrees with the experimental results quoted previously Schwan[14] has presented evidence that the blood has one tenth the resistivity of the tissues surrounding the heart Using a resistivity ratio of 0 1 in EQUATION 4

$$V = 0\,18A \ln \frac{r_1}{r_2}$$

Further work is necessary in three dimensions to test the tentative conclusion that the effect of the highly conducting blood inside the heart is uniformly to scale down the surface electrocardiograms If this proves to be correct it will be necessary to multiply the observed magnitude of the heart vector by a factor that depends on the ratio of the resistivity of the tissues surrounding the heart to the resistivity of the blood *

* Subsequent to the presentation of this article experiments with dog hearts[12] have indicated that the reduction is uniform at remote points but is variable in the vicinity of the heart

A promising analytic approach is the extension of the image system for a source in an insulating sphere[6,27] to that for a source in a sphere of finite conductivity immersed in an infinite medium of different conductivity.

(3) *Source and sink outside disk: potentials inside disk* (FIGURE 11). Again there are no images. For each position of the dipole, however, there must be added a constant potential of value $\frac{1-G}{1+G}\ln\frac{a}{b}$. The potential equation is

$$V_i = A\left[\frac{2G}{1+G}\ln\frac{r_1}{r_2} + \frac{1-G}{1+G}\ln\frac{a}{b}\right] \tag{5}$$

(4) *Source and sink outside disk: potentials outside disk* (FIGURE 12). If as a first approximation the lung sections are represented by circles, this case would

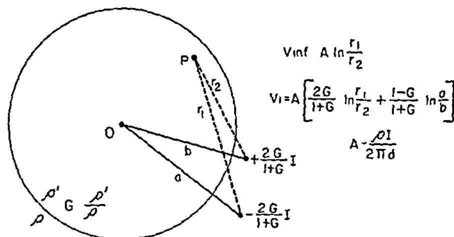


FIGURE 11. Image system for potential at P *inside* the disk due to the source $(+I)$ and sink $(-I)$ *outside* the disk.

give qualitative information about the effect of the lungs on the heart E.M.F. The sink and source are located at distances of a and b from the center of the disk. Images of strength $\frac{G-1}{G+1}I$ are located inside the disk at distances of $\frac{R^2}{a}$ and $\frac{R}{b}$ from the center. The potential equation is

$$V = A\left[\ln\frac{r_1}{r_2} + \frac{G-1}{G+1}\ln\frac{r_3}{r_4}\right] \tag{6}$$

Assuming that the lungs have a resistivity four times that of the surrounding medium, this becomes

$$V = A\left[\ln\frac{r_1}{r_2} + 0.6\ln\frac{r_3}{r_4}\right]$$

which can be compared with EQUATION 3.

EQUATION 6 indicates that the magnitude of the effect of the increased resistivity of the lung for a fixed-dipole orientation must depend on (*a*) the location of the field point at which the potential is required and (*b*) the dipole angle For example consider that the heart E M F and a lung can be represented by a dipole on the X axis and a disk whose center also lies on the X axis If the dipole angle is 0° the image dipole inside the disk will have an angle of 180 and will be oppositely directed to the real dipole This means that the potential in the region between the real dipole and the image dipole (near side of the disk) will be more positive than in the case of a homogeneous medium The region on the far side of the disk will now be less positive however because the image dipole potential partly offsets that due to the real dipole Physically these effects are caused by the current shielding properties of the disk

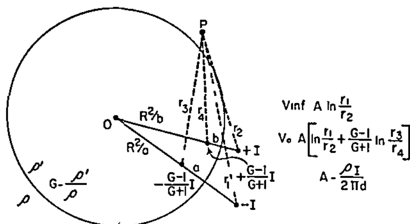


FIGURE 12 Image system for potential at *P outside* the disk due to the source (+*I*) and sink (−*I*) *outside* the disk

If the real dipole angle is 90 however the image dipole angle will also be 90° Since both dipoles have the same transverse axis the location of the zero potential line is unchanged Potentials will now be increased on both the near and far sides of the disk since the real and image dipoles reinforce each other Thus it is not possible to make a general statement about the over all effect of the higher resistivity of the lungs

In the thorax model conditions are considerably different from the artificial case of a dipole outside a disk The lung sections are not circular and they surround the heart area more completely There is also an additional shielding action caused by the spine and sternum sections It is therefore necessary to go by the model measurements although the image concept helps in interpreting the results If the main portions of the lung sections are represented by circles images inside the circles can be found for each source and sink location This approximation will help in understanding the results of TABLE 1 It should be noted that for lung resistivity ratios of 1 4 and infinity the term $\frac{G-1}{G+1}$ in EQUATION 6 has the values 0 0 6 and 1 0 Thus as the re

sistivity ratio increases the *strength* of the images increases and the lung sections have relatively more effect on the field distribution

EQUATIONS 1 4 5, and 6 were tested experimentally in the double layer tank by using disks of various thickness in the electrolyte In this way some errors were found and corrected this illustrates another use for the tank

As a further check the potential distributions for cases *a* and *b* above were calculated by the conventional method of potential theory that is by expanding the potential in an infinite series using polar coordinates and finding a solution of Laplace s equation that satisfies the boundary conditions The results were identical to those found by using Hague's simplified method

Simultaneous Effect of Lower Heart and Higher Lung Resistivities

Again we make the approximation of representing the heart and lung sections by circles The heart E M F is represented by $+I$ and $-I$ If we let G_1 equal the heart resistivity ratio then it is seen from EQUATION 4 that the inhomogeneous heart area can be eliminated by substituting $+\frac{2G_1 I}{1+G_1}$ for $+I$ and $-\frac{2G_1}{1+G_1} I$ for $-I$ Substituting these values in EQUATION 6 with G_2 equal to the lung resistivity ratio the potential at any point outside both the heart and lung areas is

$$V = \frac{2G_1}{1+G_1} A \left[\ln \frac{r_1}{r} + \frac{G-1}{G_2+1} \ln \frac{r_3}{r_4} \right] \qquad (7)$$

with $G_1 = 0\ 5$ and $G = 4$ EQUATION 7 becomes

$$V = \frac{2}{3} A \left[\ln \frac{r_1}{r_2} + 0\ 6 \ln \frac{r_3}{r_4} \right]$$

This shows that in addition to the potential changes caused by the lung sections as expressed by the second term inside the bracket there is also an over all reduction of potentials by two thirds FIGURE 7 shows that the actual reduction is about one half but that the observed reduction is uniform (the equations derived above are accurate only for a disk immersed in an infinite medium) Thus the effects of the higher resistivity of the lungs and the lower resistivity of the heart tend to counteract each other in some areas and to be additive in others since the effect of the lung sections is to increase the potential at some points and to decrease it at others

Straight Line Boundaries Between Regions Having Finite Resistivities

With straight line boundaries two image systems are necessary depending on which side of the boundary potentials are measured Consider a sink $-I$ and a source $+I$ immersed in a conducting medium having resistivity ρ which is separated from a medium of resistivity ρ by an infinite straight line For the measurement of potentials within the medium in which the source and

sink are located images must be added in the other medium at an equal distance from the boundary Then

$$V = \frac{\rho I}{2\pi d}\left[\ln\frac{r_1}{r_2} + \frac{1-G}{1+G}\ln\frac{r_3}{r_4}\right] \tag{8}$$

where again $G = \frac{\rho'}{\rho}$

For potentials in the other medium there are no images but $+I$ and $-I$ must be replaced by $+\frac{2}{1+G}I$ and $-\frac{2}{1+G}I$ Then

$$V = \frac{\rho' I}{2\pi d}\,\frac{2}{1+G}\ln\frac{r_1}{r_2} \tag{9}$$

In these equations it is assumed that all space has the resistivity ρ Diagrams of image systems for straight line boundaries as applied to nerve conduction were given by Bishop [5] A paper by Pruitt and Valencia [29] to which reference was previously made [2] gives the image system for plane boundaries and applies the method to a problem involving myocardial injury

Potential Due to a Source and Sink Inside an Ellipse Mathematical Expression

Since the thorax cross section so closely resembles an ellipse an attempt has been made to find an image system for a source inside an ellipse but this has not been successful Hicks[30] described an image system involving a line source and line doublet distribution between the foci of the ellipse but the evaluation of the potential was difficult Therefore it was necessary to expand the potential in an infinite series of elliptical harmonics using elliptical coordinates and to put in the boundary conditions that the potential V and its first derivative were everywhere continuous inside the ellipse (except at the source itself) and that the normal derivative was zero at the boundary By making an approximation leading to an error of about 1 per cent the infinite series expansion was reduced to finite form

It can be shown[31] that the relation between the elliptical coordinates u and v and the rectangular coordinates x and y is given by the equations

$$\frac{x^2}{C^2\cosh^2 u} + \frac{y^2}{C^2\sinh^2 u} = 1 \tag{10}$$

$$\cos^2 v + \sin^2 v = 1 \tag{11}$$

Then the curves u = constant are a family of ellipses with major axes on the X axis and minor axes on the Y axis FIGURE 1 shows the parameters for the ellipse chosen to represent the thorax section For this ellipse $u = u_0$ A line between the foci would represent the limiting ellipse $u = 0$ The lines v = constant represent a system of orthogonal confocal hyperbolas

The potential distribution around the periphery of the ellipse due to a source

and sink located anywhere inside the ellipse is given by

$$V_b = A \ln \left[\frac{\cosh (u_0 + u'') - \cos (v + v'')}{\cosh (u_0 + u') - \cos (v + v')}\right] \left[\frac{\cosh (u_0 - u'') - \cos (v - v'')}{\cosh (u_0 - u') - \cos (v - v')}\right] \left[\frac{\cosh (3u_0 - u'') - \cos (v + v'')}{\cosh (3u_0 - u') - \cos (v + v')}\right] \left[\frac{\cosh (3u_0 + u'') - \cos (v - v'')}{\cosh (3u_0 + u') - \cos (v - v')}\right] \quad (12)$$

where

V_b = potential at a point on the boundary of the ellipse

$A = \frac{\rho I}{2\pi d}$ and ρ = resistivity of the internal medium

u_0, v = elliptical coordinates of a point on the boundary

u', v' = elliptical coordinates of the source

u'', v'' = elliptical coordinates of the sink

The elliptical coordinates of a point can be found from[31]

$$\cosh u = \frac{r_1 + r_2}{2C} \quad (13)$$

$$\cos v = \frac{r_1 - r_2}{2C} \quad (14)$$

where r_1 and r_2 are the distances from the foci of the ellipse to the point in question and $2C$ is the distance between the foci. In FIGURE 2 the circles represent values of potential measured around the boundary of the thorax section for a β angle of 0, and the crosses are values calculated from EQUATION 12. For values of β equal to 30°, 60, and 90, the agreement was not quite as good as this but it was still within 10 per cent. The *shapes* of the measured and calculated curves agreed very closely, but the curves were shifted relative to each other. This may signify that the reference electrode was not exactly at zero potential. The field due to any number of sources and sinks can be obtained from EQUATION 12 by superposition.

The equation for the potential at any point *inside* the ellipse due to a source and sink at any two points is more complicated than EQUATION 12, but is still expressed in finite form. Thus the potential due to a source alone is given by

$$V = -\frac{A}{2} \ln [\cosh (u + u') - \cos (v + v')] [\cosh (u - u') - \cos (v - v')] [\cosh (2u_0 - u + u') - \cos (v + v')] [\cosh (2u_0 - u - u') - \cos (v - v')] [\cosh (2u_0 + u - u') - \cos (v + v')] [\cosh (2u_0 + u + u') - \cos (v - v')] [\cosh (4u_0 - u - u') - \cos (v + v')] [\cosh (4u_0 - u + u') - \cos (v - v')] \quad (15)$$

In this equation u and v are the coordinates of the point for which the potential is required A similar expression holds for the sink using u'' and v'' instead of u' and v

To illustrate the use of EQUATION 12 and the method of finding u and v the potential expression is derived for the conditions of FIGURE 1 To find the value of u_0 any point on the boundary can be used Taking the point $x = +A = 16\ 5$ and using EQUATION 13

$$\cosh u_0 = \frac{26 + 7}{19} = 1\ 74$$

$$u_0 = 1\ 15$$

Since from the definition of an ellipse $r_1 + r_2 =$ constant the same value of u_0 would be obtained for any other point on the boundary For the source

$$\cosh u' = \frac{12\ 9 + 9\ 6}{19} = 1\ 185$$

$$u' = 0\ 60$$

and from EQUATION 14

$$\cos v' = \frac{12\ 9 - 9\ 6}{19} = 0\ 174$$

$$v = -80$$

The minus sign for v is explained by the fact that the range of v is approximately the same as the corresponding polar angle Thus in FIGURE 1 v has a value between 0 and 90° in the first quadrant of the x y plane between 90 and 180° in the second quadrant etc Since the source is in the fourth quadrant it must lie in the range of 0 to −90° For the sink

$$u'' = 0\ 60$$

$$v'' = -100 = -(\pi + v)$$

Substituting the values in EQUATION 12, with $A = 1\ 0$

$$V_b = \ln\left[\frac{2\ 96 + \cos(v + 80)}{2\ 96 - \cos(v - 80)}\right]\left[\frac{1\ 16 + \cos(v - 80)}{1\ 16 - \cos(v + 80)}\right]$$
$$\left[\frac{8\ 67 + \cos(v + 80)}{8\ 67 - \cos(v - 80)}\right]\left[\frac{28\ 7 + \cos(v - 80)}{28\ 7 - \cos(v + 80)}\right] \qquad (16)$$

To find V_b for any point v is found from EQUATION 14 and used in EQUATION 16 Thus for $x = +A$ $v = 0$ Then $V_b = \ln 1\ 59 = 0\ 46$ v The measured value of potential at this point is 0 47 v

Two other equations that are useful in converting between elliptical and rectangular coordinates are

$$x = C \cosh u \cos v \qquad (17)$$

$$y = C \sinh u \sin v \qquad (18)$$

PART II THREE DIMENSIONAL STUDIES

In order to compare the two dimensional measurements with those made in three dimensions, the cross section of the deep tank had the shape of the ellipse of FIGURE 1. The tank, shown in FIGURE 13, consisted of a plastic elliptical cylinder 18 in. in depth, with the major axis of the cross section 12.6 in. (32.1 cm.) and minor axis 10.1 in. (25.7 cm.). The length of the periphery was therefore 35.9 in. (91.3 cm.). Although models fashioned after a human thorax[2,7,8] are more accurate for the specific subject, it was thought that in view of the wide variations in body build between individuals, the elliptical tank would be sufficiently accurate for most purposes. Also, it has been shown that the detailed shape of the torso is relatively unimportant.[8] I found, however, that it was necessary to retain the elliptical cross section, since a circle used to represent the thorax section gave less accurate results.

The measuring equipment was similar to that used with the flat tank,[2] except that a new type of differential amplifier was designed to couple between the search and reference electrodes and an oscilloscope. Two current electrodes were mounted in the tank in a position corresponding to that of the heart in the body, that is, nearer to the front and top of the tank. These electrodes were mounted on insulated arms that were suspended from a calibrated disk. The disk was rotatable about both the horizontal and vertical axes, so that any angle in space could be obtained. The measuring probe consisted of platinum wire soldered to the end of a length of stainless steel

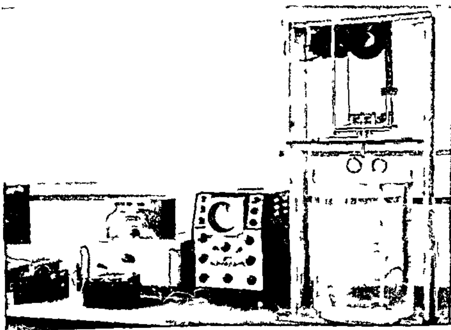


FIGURE 13. Deep tank and measuring equipment.

hypodermic needle tubing This assembly was inserted into a glass tube and the glass was sealed off around the platinum wire leaving only the end exposed By means of a sliding rod mechanism the search probe could be motor driven around the periphery of the ellipse giving the boundary potential distribution very quickly The reference electrode was a piece of platinum foil cemented to the bottom of the tank at the back

The 500 cycle search and reference voltages from the tank were connected to inputs 1 and 2 of the differential amplifier (FIGURE 14a) The voltages were amplified by the two pentodes and applied to the primary of a transformer *The output of the unit consisted of a voltage the magnitude of which with* respect to ground was proportional to the difference in voltage between the search and reference electrodes This voltage was applied to the Phase Sensitive Rectifier (FIGURE 14b) After passing through an attenuator the signal was amplified by the 6J7 and rectified by the 6H6 tube The resulting DC voltage was passed through a two-section filter and applied to the vertical input of a cathode ray oscilloscope In order to provide polarity information

FIGURE 14 Measuring circuits used with the deep tank

Part II Three Dimensional Studies

In order to compare the two-dimensional measurements with those made in three dimensions, the cross section of the deep tank had the shape of the ellipse of figure 1 The tank shown in figure 13 consisted of a plastic elliptical cylinder 18 in in depth with the major axis of the cross section 12 6 in (32 1 cm) and minor axis 10 1 in (25 7 cm) The length of the periphery was therefore 35 9 in (91 3 cm) Although models fashioned after a human thorax[2,1] are more accurate for the specific subject it was thought that in view of the wide variations in body build between individuals the elliptical tank would be sufficiently accurate for most purposes Also it has been shown that the detailed shape of the torso is relatively unimportant[3] I found however that it was necessary to retain the elliptical cross section since a circle used to represent the thorax section gave less accurate results

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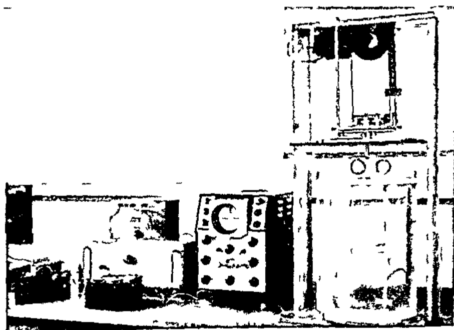


Figure 13 Deep tank and measuring equipment

hypodermic needle tubing. This assembly was inserted into a glass tube and the glass was sealed off around the platinum wire, leaving only the end exposed. By means of a sliding rod mechanism, the search probe could be motor driven around the periphery of the ellipse, giving the boundary potential distribution very quickly. The reference electrode was a piece of platinum foil cemented to the bottom of the tank at the back.

The 500-cycle search and reference voltages from the tank were connected to inputs 1 and 2 of the differential amplifier (FIGURE 14a). The voltages were amplified by the two pentodes and applied to the primary of a transformer. The output of the unit consisted of a voltage the magnitude of which, with respect to ground, was proportional to the difference in voltage between the search and reference electrodes. This voltage was applied to the Phase Sensitive Rectifier (FIGURE 14b). After passing through an attenuator, the signal was amplified by the 6J7 and rectified by the 6H6 tube. The resulting DC voltage was passed through a two-section filter and applied to the vertical input of a cathode ray oscilloscope. In order to provide polarity information

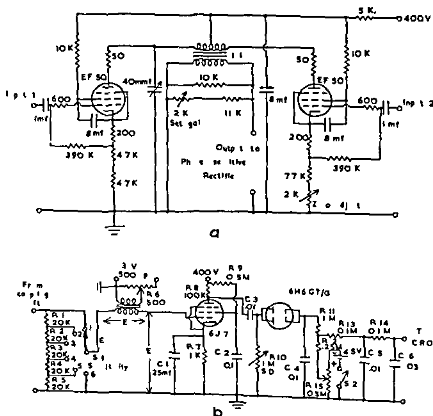


FIGURE 14. Measuring circuits used with the deep tank.

a constant 500-cycle reference voltage E was applied to the input of the 6J7 tube in series with the tank voltage E The oscilloscope controls were adjusted so that when E equalled 0 the spot was centered vertically on the screen Depending on the position of the search probe in relation to the reference electrode in the deep tank E_t was either in phase with E thereby adding to it or out of phase with E and subtracting from it In this way a plus or 'minus voltage in the tank would result in an upward or downward deflection of the oscilloscope spot The switch S2 and the 4 5 v battery shown in FIGURE 14b were used to obtain additional DC bias for the oscilloscope used but should not be needed with most commercial oscilloscopes

For horizontal positioning of the oscilloscope spot fine copper wire was wound on an elliptical form having the same eccentricity as the tank cross section A DC voltage was applied across this ellipse and as the search probe traveled around the tank periphery a spring contact tapped off a portion of this voltage and applied it to the horizontal plates of the oscilloscope Thus as the search probe moved around the tank the oscilloscope spot traveled from left to right across the screen and its vertical position was proportional to the potential produced by the dipole To obtain a record it was necessary to keep the camera shutter open for only a single revolution of the probe

Tank Results

Using this system the potential around the tank wall was measured at 12 horizontal levels for each dipole angle in space This was done for all possible spatial dipole angles at 30 intervals

The data obtained from the tank can be used in two ways

(1) Since potentials at all points on the thorax model are available for a given dipole orientation any system of vectorcardiography can be tested It is now generally agreed that the limbs have the same potential as adjoining points on the thorax so systems involving limb leads can be included In addition points on the thorax not included in one of the 12 levels can be obtained by interpolation In this way Einthoven s triangle and a modification thereof have been tested [33]

(2) By making similar measurements of the distribution of potential around the thorax for human subjects at a fixed instant of time during the cardiac cycle the spatial dipole angle of the heart vector can be estimated by determining which of the model distributions fits most closely FIGURE 15 shows the distribution of potential around the thorax at 7 horizontal levels for a normal male subject at the time corresponding to the peak of the R wave in lead II The levels were measured in centimeters above (+) or below (−) the center of excitation which is taken as 5 cm below the nipple line The levels shown were taken at $Z = +20$ $+16\,5$ $+12$ $+8\,2$ $+1\,8$ $-3\,2$ and $-9\,2$

FIGURE 16 shows the tank data for a dipole α angle of -60 and β angle of -30 The α angle is defined as the angle between the spatial vector and the horizontal *plane* The β angle following Wilson s notation is that between the projection of the vector on the horizontal plane and the $+X$ axis in the frontal plane We use the term α_F for the Einthoven angle, that is the angle

between the projection of the vector on the frontal plane and the +X axis in order to emphasize the fact that this angle is a "projected" one[33] With this system the spatial angle of the vector can be visualized easily The vector is assumed to lie parallel to the frontal plane pointing to the left side of the body and parallel to the horizontal plane that is both α and β angles of 0 It is then simply rotated through the angle β and tipped up or down through the angle α Comparing the distributions of FIGURE 16 with corresponding levels in FIGURE 15 it is evident that there is a general agreement between the curves The curves of FIGURE 15 actually lie somewhere between the graphs of FIGURE 15 and those in which both α and β angles are -30 We can therefore conclude that the spatial angle corresponding to FIGURE 15 is approximately an α angle of -45 and a β angle of -30 Both α and β should be correct to within ± 10 The curves of FIGURE 15 show evidence of the presence of local excitation processes or more than one effective dipole in the heart

FIGURE 16 is a typical tank data sheet The drawings show the *projections* of the vector on the horizontal frontal and sagittal planes With the system used the horizontal plane projection shows the true angle β but the angles in the other two projections are not generally equal to α It has in fact been shown[33] that

$$\tan \alpha_p = \frac{\tan \alpha}{\cos \beta} \tag{19}$$

Other relationships that hold in the system used are

$$\tan \alpha = \frac{\tan \alpha}{\sin \beta} \tag{20}$$

$$A = A \cos \alpha \cos \beta \tag{21}$$

$$A_y = A \cos \alpha \sin \beta \tag{22}$$

$$A = A \sin \alpha \tag{23}$$

$$A_y = A_h = \sqrt{A^2 + A_y^2} = A \cos \alpha \tag{24}$$

$$A = A_f = \sqrt{A_x^2 + A^2} = A\sqrt{1 - \cos^2 \alpha \sin^2 \beta} \tag{25}$$

$$A_v = A = \sqrt{A_y^2 + A^2} = A\sqrt{1 - \cos^2 \alpha \cos \beta} \tag{26}$$

In these equations A is the magnitude of the vector in space and A_h A_f and A are the horizontal frontal and sagittal projections respectively It is evident that it is necessary to find both α and β for a complete determination of the heart vector

FIGURE 17 shows the boundary potential and potential gradient curves for another subject also taken at the peak of the R wave in lead II Comparing these curves with the tank charts it can be determined that the α angle is -15 and the β angle is 0 FIGURE 18 shows the tank data for α and β angles of 0 An accurate mathematical treatment of the potential due to a source and sink in a finite elliptical cylinder is very difficult A solution can be approached by considering an infinite series of dipole images obtained by

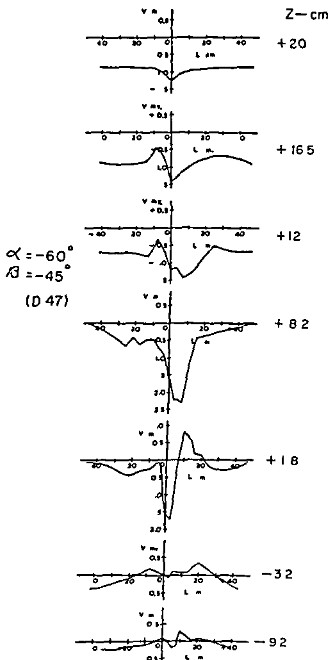


FIGURE 15 Potential distribution around the thorax of a tall thin subject at 7 horizontal levels at a time corresponding to the peak of the R wave in lead II (E M 6/12/51)

$\alpha = -60°$
$\beta = -30°$

Z – cm

12 7

10 2

7 6

5 1

2 5

0

−2 5

Potential

Distance around tank wall

−5 1

−7 6

−10 2

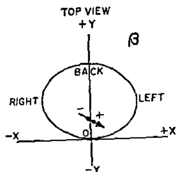
−15 2

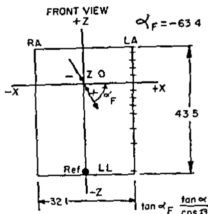
−20 3

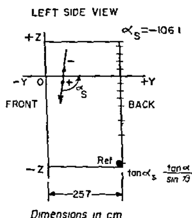
−29 7

Right – Left

Back Front Back







Dimensions in cm

FIGURE 16 Potential distribution around the wall of a deep tank at 13 different hori ontal levels The d pole angl s are (α) −o0 and (β) −30 Projections of the spatial d pole on the horizontal frontal and sagittal planes are shown to the right The angle α is the angle of the dipole with the horizontal *plane* and β is the angle between the projection of the vector on the horizontal plane and the +X axis

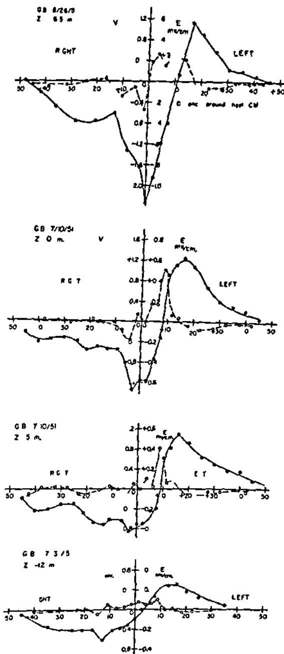
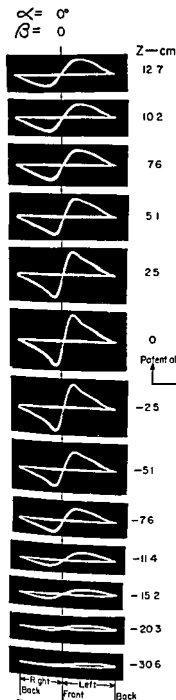
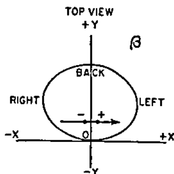
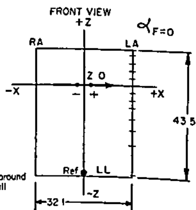


FIGURE 17 Potential distribution around the thorax of a normal male subject of medium build at 4 horizontal levels at a time corresponding to the peak of the R wave in lead II (G B 6/26/51)







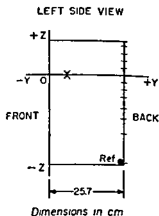


FIGURE 18 Potential distribution around the wall of a deep tank when both the α and β angles are 0°

reflections in the top and bottom surfaces[34] The image solution must then be combined with the potential distribution on the wall of an infinite elliptical cylinder

The method of showing the potential distribution over the thorax described above is in my opinion preferable to plotting the equipotentials on the thorax The former method is much easier and quicker and it provides as much information as the latter In addition the errors of measurement tend to be averaged out by drawing a smooth curve through the points Furthermore when one has the distribution of potential at several levels around the thorax one has in hand a large part of the data necessary to obtain the horizontal component of the resultant dipole moment of the heart[35] It is necessary only to multiply the potential at each point on the thorax by a factor proportional to the chest contour at that point and then to integrate the product around the chest The curve obtained by plotting potential against distance along the chest has been called the chest lead diagram[36] This type of display is deservedly becoming more popular[37-39] since time is fixed and space or distance is used as the variable

By using a chest belt with a number of small electrodes (1 cm diameter) close together (FIGURE 19) and high amplification and resolution in the recording equipment it is often possible to obtain evidence of local excitation or additional dipole components in the chest lead diagrams[13] FIGURE 20 shows the potential distributions around the chest of a normal male subject at the mid ventricular level for three different instants of time during the QRS complex The time 0 5 R would correspond to the peak of the R wave in lead 2 Local excitation processes are shown by lack of smoothness of these curves or by the presence of dips and peaks in the curves The potential gradient curves are particularly sensitive to local processes The bottom curves show a marked second dipole component

From the tank data and from theoretical considerations one can say that if

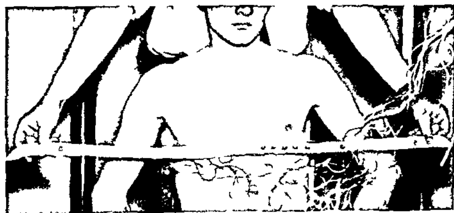


FIGURE 19 Electrode belt The electrodes are chlorided silver 1 cm in diameter The spacing at the front is 2 5 cm between centers

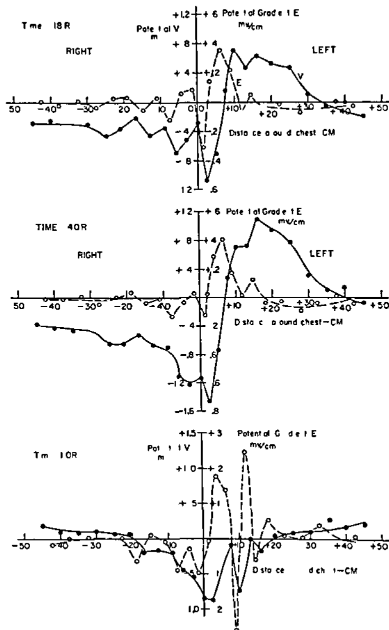


FIGURE 20 Potential distribution around the thorax at the mid ventricular level at 3 different instants of time (G B 10/7/51)

there were only one dipole acting in the heart area, there could be only one positive maximum and one 'negative' maximum of potential on the thorax wall and that the variation of potential between any two points would be continuous The same conditions would hold for the variation of potential around the thorax at any horizontal level If such graphs are not smooth curves or if there is more than one potential maximum or minimum then one must conclude that the leads are recording the effects of more than 1 dipole Whether one observes one or more dipoles depends on the number size and location of the electrodes the amount of amplification used the individual being tested and the instant of time during the cardiac cycle I have found

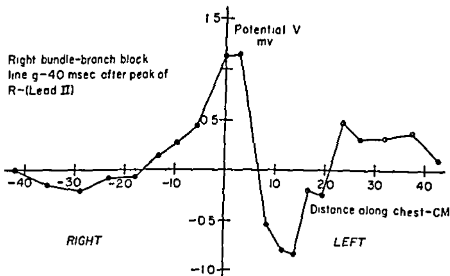


FIGURE 21 Potential distribution around the thorax at the mid ventricular level of a subject with right bundle branch block The presence of 2 simultaneous potential maxima is indicative of 2 effective dipoles in the heart (E P 2/18/55)

that in the majority of cases one major dipole component can be observed It should be noted that the method of integrating the potential over the thorax[35] gives the *resultant* dipole regardless of whether or not local excitation processes are observed in the chest leads

FIGURE 21 shows the chest lead diagram for a case of right bundle branch block at a time corresponding to 40 msec after the peak of R in lead 2 The presence of two positive and negative maxima indicates the presence of 2 effective dipoles Presumably the excitation has spread into the right ventricle and is also active in the left ventricle

If data on the potential distribution over the thorax displayed in other ways[37-41] are plotted by the method described in this paper similar results are obtained that is there is usually one major dipole but evidence of additional dipoles can occasionally be seen

Summary

The distribution of potential around the boundary of a three dimensional electrolytic tank model of the human thorax at the level of the dipole center is similar to the potential distribution around a similar flat tank if the vertical angle of the dipole is within the range of ±30° Two-dimensional thorax models can therefore provide information about the horizontal components of heart excitation

Using such a flat tank an artificial dipole was set up in the heart area and potential distributions were measured for the following four cases (1) an insulating boundary having a homogeneous interior and shaped for the outline of the thorax cross section (2) insulating spine and sternum areas inserted and lung sections having a resistivity four times that of the main body of electrolyte (3) the same as (2) except that the heart area was made more conducting and (4) the same as (2) except that the lung sections were made completely insulating

For each case the potential and potential gradient along the periphery of the model were plotted as a function of distance

The effect of the highly conducting heart section was uniformly to scale down potentials external to the heart The *effect* of increasing the relative resistivity of the lung sections depended on (1) the dipole angle and (2) the particular field point under consideration It is not possible to make a general statement about the effect of increased lung resistance since for certain dipole angles the potential was increased at some points in the field and decreased at others

For any dipole angle the differences between potentials on the outer boundary for cases 1 and 2 were not large The conductivity of the heart section had a greater effect on the boundary potentials than did the conductivities of the lungs sternum and spine sections A much larger effect was found if the lung sections were made completely insulating The effect of inhomogeneous areas on the potentials was greater in the interior of the section than on the boundary

For dipole angles of 0° to 60 the main peak of the potential gradient curve was opposite the center of the dipole For a dipole angle of 90° the potential gradient curve on the boundary was diphasic and the point of zero potential gradient was opposite the dipole center

Image systems were developed for sources and sinks in two media of *finite* resistivities separated by straight line and circular boundaries For the latter four systems were required depending on whether the source and sink were inside or outside the circle and whether potentials were required inside or outside the circle If we represent the heart area by a circle the theory showed that the effect of increased heart conductivity should cause the *external* potentials to be reduced uniformly but that the endocardial potentials would be changed in a complicated way The image theory showed that *increased* lung resistivity would also have a complicated effect on field potentials

Tests with two dipoles showed that if both dipoles had the same center, the *external field* distribution was equivalent to that produced by the resultant

dipole If one dipole was located in the left ventricular area and the other in the right ventricular area, the effect of each dipole could usually be observed on the anterior wall of the thorax section These results indicate that vector cardiograms should be supplemented with chest leads in order to obtain as complete information about the heart excitation as possible

The external field of two half shells in the heart area in the thorax section was very similar to that of the resultant dipole

Since the thorax section was almost elliptical in shape mathematical expressions were developed for the potential due to a source and sink inside an ellipse A much simpler equation resulted for potentials on the outer boundary of the ellipse

The distribution of potential around the outer wall of the three dimensional thorax model was obtained at about twelve horizontal levels for all possible spatial angles of the dipole at 30° intervals By comparing similar human thorax potential distributions with the tank charts a rapid estimate could be made of the heart vector orientation

Since such distributions give the potential at all points on the thorax they make it possible together with the limb leads to test any system of vector cardiography Equations are given for the projections of a spatial dipole in terms of its absolute magnitude and of its horizontal and vertical angles

Using a circumferential chest belt with small closely spaced electrodes evidence of local excitation in the chest lead diagram can often be seen It is pointed out that the amount of local excitation effect recorded depends on the size number and spacing of electrodes on the recorder amplification on the individual studied and on the instant of time during the cardiac cycle

Acknowledgment

I am indebted to the late Samson Wright and to W F Floyd of the Physiology Department Middlesex Hospital Medical School London England for the frequent conversations that gave me an insight into certain aspects of physiology that could have been acquired in no other way Thanks are due also to members of the staff of the Electrical Engineering Department Imperial College of Science, London particularly to Willis Jackson and to Dennis Gabor Colin Cherry and A R Boothroyd and to Allan Gordon of the Mathematics Department for advice on the problem of the ellipse I also thank Hans H Hecht for his cooperation in more recent phases of the project

References

1 Nelson C V 1952 Electric field measurements in a two-dimensional conductivity tank model of the human heart and thorax J Physiol 116 15P
2 Nelson C V 1955 The effect of the finite boundary on the potential distribution in volume conductors Circulation Research 3 236
3 Hague B 1929 Experimental methods for determining the distribution of electric and magnetic fields Electrician 102 185
4 Bewley L V 1948 Two dimensional Fields in Electrical Engineering Macmillan New York N Y
5 McFee R R M Stow & F D Johnston 1952 Graphic representation of electrocardiographic leads by means of fluid mappers Circulation 6 21
6 Brody D A & W E Romans 1954 Validity of several types of vector cardiographic

leads as tested on a two dimensional model of the human body J Appl Physiol 6 745

7 Katz L N 1937 Concerning a new concept of the genesis of the electrocardiogram Am Heart J 13 17

8 Lepeschkin E 1951 Modern Electrocardiography 55 Williams & Wilkins Baltimore Md

9 Burger H C & J B van Milaan 1943 Measurement of the specific resistance of the human body to direct current Acta Med Scand 114 584

10 Lindner E & L N Katz 1939 The relative conductivity of tissues in contact with the heart Am J Physiol 125 625

11 Hess W 1935 Modellversuche über den Verlauf der Potentiallinien des Herzens im transversalen Brustkorbquerschnitt Z Kreislaufforsch 27 433

12 Schaefer H E 1935 Versuche über neue Möglichkeiten die Richtung der Aktion pol im Herzen zu bestimmen Z Kreislaufforsch 27 439

13 Nelson C V & H H Hecht 1955 Investigation of horizontal component of heart vector by means of circumferential chest leads at midventricular level Federation Proc 14 107

14 Lepeschkin F 1951 Modern Electrocardiography 43 Williams & Wilkins Baltimore Md

15 Frank E & C F Kay 1953 A reference potential for unipolar electrocardiographic measurements on models Am Heart J 46 195

16 Sugi Y 1940 Studies on the origin of the injury potential of muscle Japan J Med Sci III 6 293 331

17 Kaufman W & F D Johnston 1943 The electrical conductivity of the tissues near the heart and its bearing on the distribution of the cardiac action currents Am Heart J 26 42

18 Schwan H P & F C Kay 1956 The conductivity of living tissues Ann N Y Acad Sci 65 (6) 1007

19 Belehradek J & A K M Novo s 1933 L électrocardiogramme du coeur perfusé au glucose Compt rend soc biol 88 621

20 Straub H 1910 Zur Analyse des Elektrokardiogramms nach Versuchen am isolierten Froschherzens Z Biol 53 499

21 Katz L N E Sigman I Gutman & F H Ocko 1936 The effect of good electrical conductors introduced near the heart on the electrocardiogram Am J Physiol 116 343

22a Burger H C & J B van Milaan 1946 Heart vector and leads Part I Brit Heart J 8 157

22b Burger H C & J B van Milaan 1947 Heart vector and leads Part II Brit Heart J 9 154

22c Burger H C & J B van Milaan 1948 Heart vector and leads Part III Brit Heart J 10 229

23 Lewis T 1925 The Mechanism and Graphic Registration of the Heart Beat The duality of the normal electrocardiogram 104 Shaw & Sons 3rd ed London England

24 Rijlant P 1933 L'oscillogramme cathodique du coeur humain Compt rend soc biol 114 546

25 Hague B 1929 Electromagnetic Problems in Electrical Engineering Oxford Univ Press Oxford England

26 Hicks W M 1880 On the motion of two spheres in a fluid Trans Roy Soc 171 455

27 Ludford G S S J Martinek & G C K Yeh 1955 The sphere theorem in potential theory Proc Cambridge Phil Soc 51 389

28 Bishop G H 1937 La théorie des circuits locaux permet-elle de prévoir la forme du potentiel d action? Arch intern physiol 45 273

29 Pruitt R D & F Valencia 1948 The immediate electrocardiographic effects of circumscribed myocardial injuries an experimental study Am Heart J 35 161

30 Hicks W M 1881 On functional images in ellipses Quart J pure appl Math 17 327

31 Weber Ernst 1950 The Electromagnetic Field 1 Mapping of Fields Wiley New York N Y

32 Frank F C F Kay G E Seiden & R A Keisman 1955 A new quantitative basis for electrocardiographic theory the normal QRS complex Circulation 12 406

33 Nelson C V & H H Hecht 1955 A test of the Einthoven triangle and a [illegible] which corrects for the lateral eccentricity of the heart Circulation 12 752

34 Burger H C H A Tolhoek & F G Backbier 1954 The potential distribution on the body surface caused by a heart vector Am Heart J 48 249
35 Gabor D & C V Nelson 1954 Determination of the resultant dipole of the heart from measurements on the body surface J Appl Phys 25 413
36 Lepeschkin E 1951 Modern Electrocardiography 83 Williams & Wilkins Baltimore Md
37 Bohning A L N Katz & R Langendorf 1941 The distribution of surface potential on the chest in intraventricular block Am Heart J 22 778
38 Simonson E 1952 The distribution of cardiac potentials around the chest in 103 normal men Circulation 6 201
39 Gillmann H 1952 Differenzierung der formgestaltenden Kräfte der unipolaren Brustwandableitungen Cardiologia 20 314
40 Osher, H L & L Wolff 1953 Electrocardiographic pattern simulating acute myocardial injury Am J Med Sci 226 541
41 Sikand R S A Mauro & L H Nahum 1952 Instantaneous distribution of the electrocardiographi potential on the body surface of the normal man during the T interval J Appl Physiol 4 916
42 Nelson C V R L Lange, H H Hecht R P Carlisle & A S Ruby 1956 Effect of intracardiac blood and of fluids of different conductivities on the magnitude of surface vectors Circulation 14 977

DISCUSSION PART IV

L N Katz *Chairman*

D A Brody (*Division of Medicine University of Tennessee Memphis Tenn*) The articles by Johnston and Frank are prime examples of the type of progress that has been made in the heart lead relationship since L N Katz first raised his voice against the authoritarianism of the equilateral triangle some twenty years ago

In regard to Johnston s article I believe that the lead field provides the most comprehensive single concept of the heart lead relationship that has ever been advanced In support of this seemingly extravagant appraisal I present the following bill of particulars

(1) All of the essentials and most of the particulars of lead vector theory are imbedded in the lead field theory

(2) The lead field supplants and generalizes the solid angle concept In this respect the lead field has as its mathematical basis the divergence theorem of vector calculus whereas the solid angle concept is based on the Gauss theorem Therefore the solid angle concept is a special case of the lead field just as the Gauss theorem is a special case of the divergence theorem

(3) It may be shown by means of the lead field theory that the total electrical moment produced by myriads of sources and sinks within a homogeneous volume conductor is equivalent to a surface integral involving the potentials and the unit normals of the surface This approach provides an alternative derivation of the relation which Gabor and Nelson[1] deduced two years ago by means of Green s theorem and it is a confirmation of this phase of their work

(4) So-called unipolar and augmented unipolar leads are shown by means of lead fields to be of essentially the same genre as bipolar leads and thus may be relegated to their proper role in the scheme of things In my view any special merit of these leads is clearly fortuitous and not due to their alleged or possible unipolarity

(5) The inhomogeneity problem is also imbedded in the lead field theory Unfortunately however there seem to be many practical difficulties in working out satisfactory solutions

Our own interest in lead fields has been for the purpose of confirming and extending the observations of McFee and Johnston

The isoflow function of the lead fields such as demonstrated by Johnston and as shown in FIGURE 1 for lead 2 in our own model is generally difficult to map precisely in the two dimensional case and probably impossible in the three dimensional situation Therefore we prefer the simpler method of mapping the isopotential distribution which is the conjugate function of the isoflow function (FIGURE 2) More important than the relative technical simplicity however is the highly significant relationship evidenced by the fact that the direction of the lead vector (shown here in the center of the ventricular mass) is normal to the isopotential curve and the magnitude is inversely proportional to the spacing between the isopotential intervals A clear appreciation of lead vector variability over the entire cardiac region may be gained by the

simple visual inspection of an isopotential plot such as shown in this figure. This property is not wholly shared by the isoflow plot of the same lead field.

We have also been interested, as have McFee and Johnston, in tailoring lead connections in order to approximate the ideal condition of uniform lead fields. In this phase of the work FIGURE 3 shows the best result we achieved for leads designed to record accurate vectorcardiograms from our model. Although this was the result of cut and try methods, we felt that it was a reasonable approximation to the ideal configuration of uniform rectilinear squares.

More recently, we have become interested in the possibility of applying ideal lead connections to irregularly shaped volume conductors on the basis of predetermined principles rather than by trial and error methods. We believe that our approach is correct as evidenced by the strikingly uniform lead field in the peculiarly shaped model shown in FIGURE 4.

FIGURE 5 shows half of a circular model to which equally weighted electrodes were applied at equal intervals on the periphery. Although this method of electrode application has been considered elsewhere,[2] it appears to be incorrect as evidenced by the curvature of the associated lead field. The situation can be corrected, however, by weighting the electrodes in a manner determined by theoretical considerations (FIGURE 6). FIGURE 7 shows that in the two-dimen-

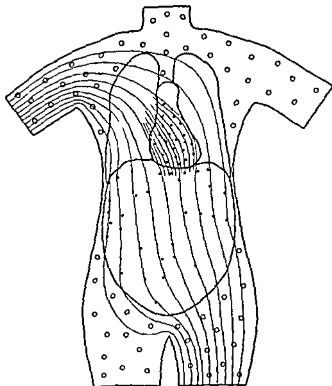


FIGURE 1

sional case a surprisingly small number of electrodes is required to obtain a lead field of good quality and that the size of the electrodes is not especially important Translating this result to the three dimensional situation we feel that an array of sixteen to twenty electrodes each applied to both the front and back of the thorax would provide an approximately ideal lead connection for recording the sagittal component of effective heart vectors

Frank s studies have produced some powerful evidence in support of the equivalent-dipole concept The validity of this concept appears to depend upon whether body surface electrocardiographic potentials satisfy the Laplace equation in a homogeneous medium with a fixed location singularity even though the Poisson equation in an inhomogeneous medium is the correct theoretical basis Frank s data indicate that the Laplace treatment results in a good first approximation for clinical purposes

The cancellation technique which is a keystone of the equivalent cardiac dipole hypothesis has some interesting clinical implications On the basis of cancellability it would seem that proximity leads do not possess any special clinical value or significance However a study which is presently being conducted in our laboratory indicates that proximity leads are of special importance in at least one type of heart disease As a matter of fact we have been able to show theoretically and in a few pilot experiments that cancellability depends

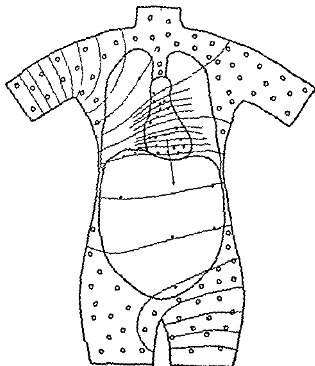


FIGURE 2

FIGURE 3

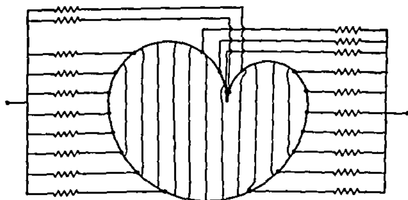


FIGURE 4 From Daniel A Brody *American Heart Journal* 1957 Vol 53 p 174

upon a number of factors other than the validity of the equivalent cardiac dipole hypothesis Therefore we are not willing to accept the thesis that semi direct leads are of the same genre as extremity leads and we are suspicious of the validity of vectorcardiographic registration systems that imply that these two types of leads are similar

Frank s demonstration of the equivalent cardiac dipole appears to contradict

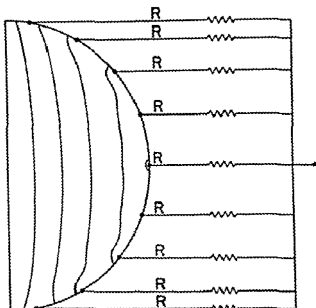


FIGURE 5 From Dan el A Brody *An erican Hea t Jou nal* 195 Vol 53 p 174

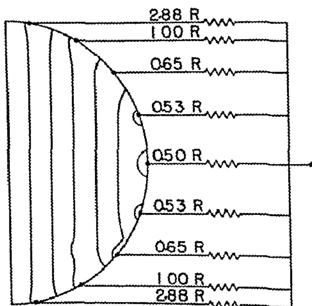


FIGURE 6 F om Dan el A Brody *Amer can H a t Jou n l* 1957 Vol 53 p 174

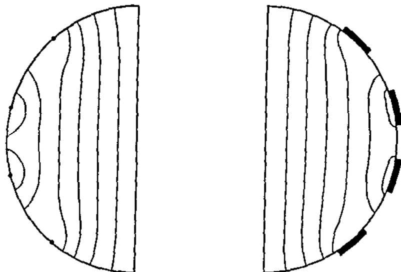


FIGURE 7 From Daniel A Brody *American Heart Journal* 1957 Vol 53 p 174

our belief that there is no such entity as a mean lead vector except in the presently hypothetical case of ideal lead connections Unfortunately, time does not permit an analysis of the factors that show that this conflict is more apparent than real

Finally, there is the intriguing question Does the equivalent cardiac dipole closely represent the *true* electrical moment of the heart? I suspect that it does not but in our present state of knowledge I do not believe that we really know

References

1 GABOR D & C V NELSON 1954 Determination of the resultant dipole of the heart from measurements on the body surface J Appl Phys 25 413

2 HELM R A 1955 The lead vectors of multiple dipoles located on an electrically homogeneous circular lamina Am Heart J 50 883

J MARTINEK AND C C K YEH (*Reed Research Foundation Washington D C* *) A survey of the present state of the art in the mathematical theory of electrocardiograms has been presented in two recent papers [1,2] It is the purpose of this discussion to complement these surveys to review some new theorems in potential theory recently published by us and by G S S Ludford that we regard as worthwhile contributions to the mathematical theory of electrocardiograms, and to outline current and intended future research in this field

Our paper in this section of the monograph represents a mathematical formulation for a singularity and a body shape of considerable generality With this series formulation the potential at any point inside or on the surface of any

* This investigation was supported by Research Grant H 2263 from the National Heart Institute of the National Institutes of Health Public Health Service Department of Health Education and Welfare Bethesda Md

prolate spheroidal body due to a dipole of any strength and any direction located at an arbitrary point in the body can be computed immediately. The extension of this analysis to any oblate spheroidal body is straightforward.

For the limiting case of a spheroid of zero eccentricity e, a better formulation, the "Interior Sphere Theorem," has been published[3] as an extension of Weiss's (exterior) Sphere Theorem.[4] This formulation is in closed form, which applies to any type of singularity (not limited to a dipole). When the singularities lie near the sphere, series form solutions converge slowly and are unsuited for numerical computation. A closed form solution, therefore, provides a powerful tool in spite of the simplicity of the body shape. This important aspect was fully realized by Wilson,[5] but it seems to have escaped general attention.

Based on the Interior Sphere Theorem, closed expressions for the potentials due to a source sink pair, a dipole, and a circular vortex ring have been calculated.[6] A human heart is representable by a combination of sources, sinks, dipoles, vortices and/or higher derivatives (higher order singularities) thereof. Potentials due to singularity combinations of various strengths and locations inside the spherical body can be obtained from these expressions. Similarly, the expressions for a general dipole that we have presented in our paper and Wait's expressions[7] for a source sink pair will provide potentials due to various singularity combinations inside any spheroidal shape.

When the conductivity of the air or other media surrounding the body is considered, a more general boundary condition must be used. A general sphere theorem for hydrodynamics, heat, magnetism and electrostatics has been worked out.[8, 9] This can be used to improve the analyses that are carried out without considering the surrounding media.

An important problem as to whether the potential measurements on a body surface can uniquely predict the inside singularities has been partly answered by a proof of uniqueness recently completed by Reed Research, Inc.[10] According to this proof, if the singularity is located at a given point inside a sphere, one surface potential distribution corresponds to one and only one type of singularity or singularity combination at that point. Under investigation now is the problem of the number of surface measurements that can determine uniquely, if possible, the location, strength, and direction of a singularity inside the body.

Three approaches are under consideration for body shapes that are more general than spheroids. One of these involves the use of integral equations.[11] Another makes use of Muller's[12,16] solutions and our approach[16, 17] using source sink methods to solve the axial flow (exactly) and the cross flow (approximately) past a body. The third approach uses near sphere and near spheroid theorems.[18, 19] Another study is the Registration Function suggested by Stallmann.[6]

In order to approach more realistically the internal structure of the human torso, we have developed a double sphere theorem.[1, 21] Two-dimensional problems are solved immediately by using the internal circle theorem[2, 22] and axial symmetric cases applicable to certain animals have been treated.[5, 4, 9]

The present outlook for exact mathematical solutions of the finite conductor problem in reference to the physics of the human heart and torso is good. It

is our opinion that in the near future workable solutions will be available and will considerably further our understanding of the problems of diagnosis

References

1 NELSON C V 1955 Effect of the finite boundary on potential distributions in volume conductors Circulation Research 3 (3) 236–42
2 HECHT H H 1955 Editorial Research in electrocardiography Circulation Research 3 (3) 231–35
3 LUDFORD G S S J MARTINEK & G C K YEH 1955 The sphere theorem in potential theory Proc Cambridge Phil Soc 51(2) 389–393
4 WEISS P 1944 On hydrodynamical images arbitrary irrotational flow disturbed by a sphere Proc Cambridge Phil Soc 40 259–261
5 WILSON F N & R H BAYLEY 1950 The electric field of an eccentric dipole in a homogeneous spherical conducting medium Circulation Research 1 89
6 YEH G C K J MARTINEK & G S S LUDFORD 1955 The potential due to certain singularities in the presence of a fixed sphere J Soc Indust & Appl Math 3(3) 142–152
7 WAIT J I 1953 Potential of two current point sources in a homogeneous conducting prolate spheroid J Appl Phys 24 (4) 496
8 YEH G C K J MARTINEK & G S S LUDFORD 1956 A general sphere theorem for hydrodynamics heat magnetism and electrostatics Z angew Math Mech 36(3–4)
9 WEISS P 1947 Applications of Kelvin s transformation in electricity magnetism and hydrodynamics Phil Mag Series 7 38 200–214
10 MARTINEK J G C K YEH & H ZORN 1955 On Uniqueness of Surface Potential Distributions Research Notes Reed Research Inc Washington D C
11 BERGMAN S & M SCHIFFER 1953 Kernel Functions and Elliptic Differential Equations in Mathematical Physics 124 Academic Press New York N Y
12 MULLER W 1951 Lang bewegung eines Rotationskorpers in der Flu sigkeit Ingr Arch 19 282–295
13 MULLER W 1952 Bewegung des langgestreckten Rotationskorpers in einer zur Langs achse geneigten Richtung Ingr Arch 20 57–66
14 MULLER W 1954 Die Bewegung eines Rotationskörpers in der reibunglosen Flussigkeit und das instabile Moment der Druckkrafte Österr Ingr Arch 8 (2–3) 171–184
15 MULLER W 1955 The effect of an enlarged head on the inertia coefficients and yawing moment of a body moving in a fluid (In German) Österr Ingr Arch 9 (1) 1–11
16 YEH G C K & J MARTINEK Singularities inside a certain class of arbitrary bodies of revolution To be published
17 MARTINEK J & G C K YEH Singularities inside a certain class of arbitrarily shaped boundaries To be published
18 POWER G 1954 Some perturbed electrostatic fields Pacific J Math 4 (1) 79–98
19 POWER G 1955 A general mathematical treatment applicable to certain electrode systems Brit J Appl Phys 6 (7) 245
20 STALLMANN F 1955 Zur mathematischen Theorie des Electrokardiogramms Z angew Math Mech 35 (9–10)
21 LUDFORD G S S G C K YEH & J MARTINEK The double sphere theorem in potential theory To be published
22 LUDFORD G S S J MARTINEK & G C K YEH The stream function for the axial symmetric flow between two concentric spheres To be published
23 MILNE THOMSON L M 1940 The circle theorem Proc Cambridge Phil Soc 36
24 HUBER A 1953 Die Randwertaufgabe der Geoelektrik für Kugel und Zylinder Z angew Math Mech 33 (10–11)
25 FRANK E 1952 Electric potential produced by two point current sources in a homogeneous conducting sphere J Appl Phys 23 1225
26 ZENKIN A 1947 The flow around a sphere in the presence of a vortex ring (In Russian) Doklady Akad Nauk S S S R 58 373–375
27 BUTLER S F J 1953 A Note on Stokes s stream function for motion with a spherical boundary Proc Cambridge Phil Soc 49 169–174
28 OLLENDORFF F 1952 Berechnung magnetischer Felder 100 Springer Verlag Wien Austria
29 SADOWSKY M A & E STERNBERG 1950 Elliptic integral representation of axially symmetric flows Quart Appl Math 8 (2) 113

E Simonson (*Laboratory of Physiological Hygiene University of Minnesota Minneapolis Minn*) I am very pleased to see that Ernest Frank has in his more detailed analysis confirmed our conclusions[1-3] that in normal subjects approximately 90 per cent of the surface potentials can be canceled and that consequently they can be accounted for on the basis of the dipole hypothesis We also obtained good cancellations in patients with various types of pathology (myocardial infarct, right and left ventricular strain and right and left ventricular preponderance) but on the average the cancellations were somewhat poorer in patients than in normal subjects We also obtained numerous excellent cancellations of the T wave usually in locations close to but not identical with those for QRS cancellation The results of T wave cancellations were not quantitatively evaluated but in many subjects the T wave cancellation was even better than the QRS cancellation

Recent experiments by Otto Schmitt and myself throw some light on this situation While it is probable that one could find a single dipole representation for the whole heart activity that would be reasonably accurate for any *instant during the heart cycle its position would necessarily change constantly* and would change differently according to the lead system utilized It has been our objective to develop leads that would make it no longer necessary that the heart be represented by a localized dipole, but by which any distribution of dipole sources in the heart region would automatically be represented correctly The distortion factor in many leads particularly in the precordial leads is tremendous We have not changed our opinion that the results of the cancellation experiments are incompatible with the concept of unipolar electrocardiography based on the concept of local patterns This is a crude oversimplification although the representation of various parts of the heart differs in different leads all parts of the heart and not only those closest to the electrode are involved in the resulting pattern in any lead location

References

1 Schmitt O H R B Levine & E Simonson 1953 Am Heart J 45 416
2 Levine R B O H Schmitt & E Simonson 1953 Am Heart J 45 500
3 Simonson E O H Schmitt R B Levine & J Dahl 1953 Am Heart J 45 655

C F Kay (*University of Pennsylvania College of Medicine Philadelphia Pa*) In his article Nelson has described a technique that he feels will define whether one is dealing with single or multiple dipoles He considers departure from the smoothness of the potential curve as evidence of the presence of more than one effective dipole I should like to study this material more thoroughly The conclusions drawn from Frank s work on humans are contrary to those of Nelson with different techniques indicating that in the great majority of human subjects one is dealing with a single equivalent dipole This is an extremely important difference and it is my feeling that it may be found that the observations of Nelson Floyd and Hecht on the human can be alternatively explained on the basis of variation in dipole moment or by definition of the problem in three dimensions whereby a straight line may cross and recross an isopotential line several times

It is certainly interesting to me to look at Nelson s illustrations and see the relatively small effect on current distribution of a four to one resistivity difference in the lung It always has seemed reasonable that the lung should have a higher resistivity than the body tissues but because of the high blood content of the lung the difference is not great I think that Schwan perhaps would admit a 10 to 20-per cent difference between the lung and other visceral tissue but this difference is too small to be statistically significant from our data

A word about capacity as stated by Schwan the capacity of tissues is sufficiently small to make phase shift an inconsequential problem in electrocardiography It might be of sufficient magnitude however appreciably to influence the high frequency components in the range of perhaps 300 cps and upward Such frequencies exist in the heart signal

The problem of inhomogeneity of living body tissues is a venerable one Our conclusion is very similar to that reached a decade ago by Kaufman and Johnston—that except for blood fat and bone the specific resistivities of body tissues are remarkably similar

I should like to define certain limitations in the significance of inhomogeneity First, what could be the influence of inhomogeneity upon the equivalent dipolar assumption? If inhomogeneity in the tissues surrounding the heart were very gross indeed the dipolar assumption might become such an approximation that electrocardiography as a field analysis problem would have little meaning Most of the evidence indicates that the signals recorded at the body surface are of a kind expected to be derived from a single fixed equivalent dipole Indeed this may be so because of the major inhomogeneity within the heart concentrating the field in the intracardiac blood

Second what may be the significance of inhomogeneity as it relates to our ability to measure the orthogonal components of the heart vector? Again if there were gross inhomogeneity the problem would become quite complicated I was surprised to learn from Nelson s figures that the problem was not more complicated than it is The methods now employed for the measurement of the orthogonal components of the heart vector are relatively independent of the inhomogeneity of the tissues that surround the heart This has been made clear two or three times in this monograph It is not implied that inhomogeneity outside the heart has no influence upon the electrical field but if it is our objective to measure the orthogonal components of the equivalent heart vector then inhomogeneities of tissues outside the heart apparently are of relatively small significance

Finally what may be the significance of inhomogeneity in the relation of the equivalent dipolar components as measured at the body surface to the actual generators of the heart? Even if we were dealing with a perfect equivalent dipole and its components could be recorded with complete accuracy electrocardiography would retain a large element of empiricism A very large number of heart generator combinations could result in the same identical heart vector This is a difficulty already painfully evident in clinical electrocardiography Perfect measurement might well narrow the range of normal patterns or delineate specific pathological entities with better definition but empiricism would remain The relation of the equivalent dipole and the generating sources in

the heart are undoubtedly influenced tremendously by inhomogeneities within the heart and by their geometric relations to each other and to the generating ources Inhomogeneities outside the heart will in this problem be relatively less significant Much further exploration of the relation of the actual heart generators to the equivalent dipolar representation is urgently needed

K S Cole (*National Institutes of Health Bethesda Md*) Those who have had much to do with impedance will probably agree that a little of it is a dangerous thing I have had a lot to say about impedance and that too is dangerous but I think that the more information we are able to obtain in the various phases—and of course one of the obvious important ones is the re covery phase—the better off we are On the other hand, it has been seen that any information is worth just about what it costs to obtain Although an impedance can give the motion of all the ions crossing a membrane this sum alone is not an analysis of the components It is unfortunate for this analysis that a heart fiber is not more like a squid axon where the framework is more certain but the squid has shown that the information can be procured

When the first measurements were made of the *in situ* impedance characteris tics of the tissues near the heart I confidently predicted that nothing new would be found below a thousand cycles Then the squid axon came along and showed fantastic things happening below that limit and the basis of my prediction was completely destroyed But nobody caught up with me until I talked Schwan into measuring muscle more carefully and he found not only that I had indeed been wrong but also that the difference was not important to cardiology

The assumption of a uniform resistance is very helpful in applying the field equations to tissue problems but the anisotropy of skeletal muscle may require more attention than has been paid to it in the past The measurements usually quoted are those in which the current flow has been perpendicular to the axis of the fibers The ions become very crowded going between the fibers and it is almost impossible to get any current flow through the interior at low fre quency If on the other hand current parallel to the fibers easily enters into the interspaces the ions antisocial and crowded into the space of a few milli meters will enter the myoplasm and give an increased conductivity simply because the cross section of the area into which they can penetrate is greatly enlarged

H C Burger (*Department of Medical Physics Physical Laboratory of the University of Utrecht Utrecht The Netherlands*) Schwan s measurements are very accurate and I am sure that what he has found is correct On the other hand, we measured the resistivity of the muscles of our own bodies years ago and we found quite different values What can be the cause? We did this with zero frequency on direct current and avoided the influence of polarization at the electrodes It was the classic method We made a current flow through a conductor by applying two current electrodes at two points thus enabling us to measure the voltage between two other electrodes When the instrument with which we measured the voltage had a sufficiently high resistance the

polarization in these electrodes had no influence at all In this way we had measured the resistivity of this conductor by measuring the current and voltage on a section of this conductor In doing so however we found a specific resistivity that was much lower than that found by Schwan

This disagreement could be solved in two ways We would repeat Schwan's measurements or Schwan could repeat our measurements I shall not say the first is impossible, but it would take much time With the proper equipment however the second course would be very simple and I am convinced that Schwan can make these measurements in a few days or in perhaps an even shorter period Therefore I should like to ask him if he would make these measurements on the muscles of his own arms or legs and see what he finds and then we shall talk further

As to Nelson's measurements my first impression is that measurements on two-dimensional objects can be very useful in giving us a qualitative idea On the other hand the time for qualitative measurements has passed We need quantitative results We know now that work such as that presented by Nelson is possible and I hope that in the future this idea will be applied to three dimensional models

L N Katz (*The Cardiovascular Department Medical Research Institute Michael Reese Hospital Chicago Ill*) I should like to take this opportunity to say that I think history will show that we have in H C Burger another Hollander who will leave a tremendous imprint on science and that the Burger triangle may ultimately and to everyone's satisfaction replace what was useful to the last generation the Einthoven triangle

Also I should like Schwan to remember that once my colleagues and I put rubber sheeting between the heart and various parts of the dog's chest and that only when the rubber sheeting was between the muscles of the backbone and the heart was there a sharp reduction in amplitude With the chest closed and the rubber sheeting between the lungs and the heart no significant difference could be observed I put it to you as has Burger that extrapolation of measurements to electrocardiographic frequency may be deceptive

Pierre Rijlant (*University of Brussels Brussels Belgium*) Some work has been going on in my laboratory on the distribution of potentials in two or three-dimensional finite media surrounding the isolated heart We have confirmed the quite classical notion that the distribution is very much modified by the limits of the conducting medium when its radius is not more than threefold that of the centered heart When the radius is about five times that of the heart the distribution of potentials is quite independent of the limitation of the extent of the conducting medium

This monograph has covered many different aspects of that same problem It has been shown that even in a finite conductor the influence of the boundaries can be reduced by adequate methods such as the use of loaded leads We thought it would be worthwhile to aim in another direction starting from some observations made by Wilson who admitted that the increase of the volume of the conducting medium surrounding the heart should have a favor

able action We tried to duplicate a three dimensional nonfinite conducting medium by closing a network of resistances in such a way that it became equivalent to an infinite-conducting three-dimensional medium

The potentials were led off from the thoracic surface through a large number of regularly spaced electrodes and were fed to the resistive network Potential measurements in different locations inside the network at a distance from the multiple input yielded values that allowed a vectorgram to be constructed These values were similar to those obtained in an infinite conducting medium at a distance at least five times the radius of the heart The shape and size of vectorgrams constructed for different orientations in the same plane are nearly identical this fact emphasizes the regulating action of the resistive network

O H Schmitt (*University of Minnesota Minneapolis Minn*) Cancellation theory was developed to permit experimental justification of the lumped dipole source approximation that is so essential to most present-day electrocardiographic theory It is generally conceded that the heart is never exactly equivalent to a dipolar source but authorities differ considerably in the emphasis they give to the deviations Those anxious to consider the heart as a concentrated source at an anatomically locatable position emphasize the smallness of the portion of the total source moment (approximately 10 per cent) that cannot be reconciled with this hypothesis Those anxious to stress the predominance of adjacent heart tissue in contributing to potential developed at a surface lead emphasize the substantial difference in attenuation (typically 2 1 or 3 1) between similarly disposed nearest and most distant heart regions

It seems appropriate in this discussion to point out three factors that are not immediately evident from mirror pattern or cancellation types of thinking In the first place it is often erroneously supposed that the Wilson central terminal (or other references developed by combination and weighting of surface potentials) is electrically equipotential with some anatomical point preferably near the center of the heart This is not even approximately true for the actual case of a finite heart and it might be profitable for some who still believe in this notion to look for the null anatomic point experimentally with catheter or plunge electrodes so that they might see how poor this equivalence actually is

Second the cancellation experiments that have suggested exact localization of an equivalent dipole source have led some investigators to assume that the source positions thus found are intrinsically localized in as precise a manner The dipole loci are indeed precisely specifiable as demonstrated by Frank s excellent work but the precision of location and indeed the place at which localization occurs depend primarily not alone on the anatomy but on the leads utilized and the exact pathways of excitation of the heart for the beats analyzed Thus appreciably different dipole source loci will be found for alternate beats utilizing different pathways and even the same beats give different centers for the QRS and the T waves

Finally we realize as carefully chosen leads are developed that *de emphasi e* skewing and proximity effects that the source dipole becomes very poorly localizable Far from being desirable a lead system that allows exact localiza

tion of a dipole center is a bad lead system from the point of view of uniform orthogonal representation of all regions within the heart. If a really ideal lead system were derived it would represent every region within the possible heart volume exactly equally and in exactly equivalent direction and would, by proper cancellation techniques, yield a dipole center completely ambiguous in its location.

A. M. SCHER (*University of Washington, Seattle, Wash.*): In what we refer to as dipole experiments we place a number of 4 mm. bipoles in line into the heart of a living animal and measure the body surface potential distribution resulting from each. FIGURE 1 shows the potential distribution on the body surface resulting from a single bipole lying in the left ventricular wall. The detailed study which will include bipoles placed in three planes and moving in those planes is just getting under way. From the results so far two things can be stated.

First, if the value of the maximum potential at the body surface from a number of bipoles in line (the maxima will fall at the same point) is plotted as a function of distance between the bipole and the body surface point, the fall off is not what would be expected from a bipole in a homogeneous medium.

Second, as can be seen in the figure, the value of the potential on the body surface from a given intracardiac bipole can fall off very rapidly as a function of distance from the point of highest voltage. In other words, looking at the figure, we might consider the maximum negative value of 120 units to be produced by an infarct localized at the bipole center in the left wall. If we should move our recording terminal 2 inches nearer the sternum, the potential would be only 21 units and therefore we should have much less chance of picking up the infarct.

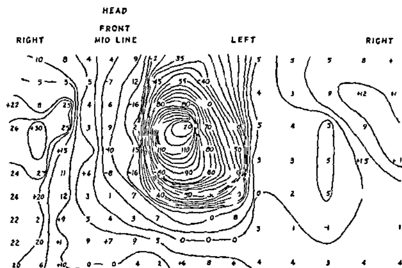


FIGURE 1

Although it is too early to make a definite statement based on our results it is our feeling that despite its simplicity and obvious usefulness as an approximation the substitution of a single equivalent dipole for the complex system of boundaries within the heart during ventricular depolarization is an oversimplification that will be most likely to give false answers about infarction

R A Helm (*Department of Internal Medicine University of Cincinnati College of Medicine Cincinnati Ohio*) I wish to congratulate Nelson for his lucid demonstration of the effect of boundary contour on the distribution of dipole potentials and I should like to describe certain calculations I have made relating to this problem

Four dipole locations corresponding to the 00- 08- 80- and 66-dipole locations of Frank s model were chosen for consideration (figure 1) It can be noted that there are 16 boundary points A through P distributed about the periphery of Frank s torso model at the same transverse level as the plane on which the dipoles are located The object of this study was to determine the effect of varying the contour of the boundary while the locations of the 4 dipoles and of the 16 points were held constant In order to accomplish this objective

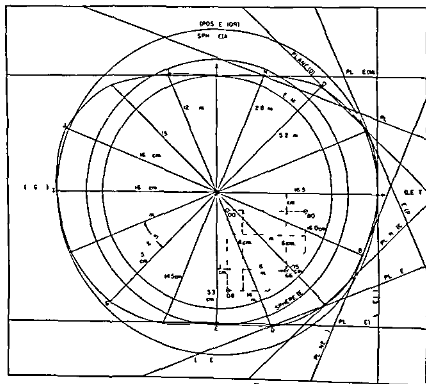


Figure 1

the potentials developed at each of the 16 points *A* through *P* were determined for each of the 4 dipoles acting separately, when the following boundary conditions were assumed

(1) A *single* infinitely large plane existing consecutively at each one of the 16 points *A* through *P*, at the time the potential at each point was calculated. As noted in FIGURE 1 which illustrates the plane in 9 of its 16 different positions such a plane is always perpendicular to the radius from the center of the section to the point in question

(2) A *single* sphere that like the plane exists consecutively at each one of the 16 points at the time the potential at each point was calculated (3 such spheres are shown in FIGURE 1)

(3) The boundary contour of Frank's torso model which as illustrated in FIGURE 1, exists simultaneously at each of the 16 points

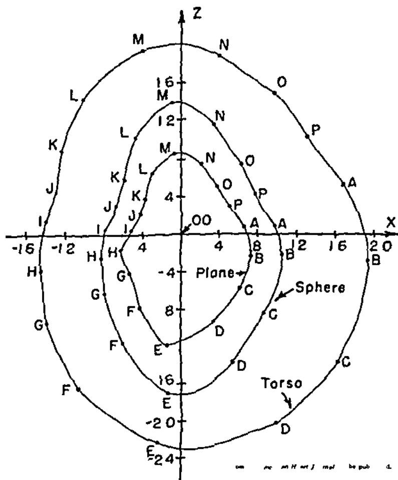


FIGURE 2

The calculations for the planar and spherically bounded media were made by means of the Wilson Bayley equations The data published by Frank were utilized for the torso boundary In all cases the medium was assumed to be homogeneous with a resistivity of 1000 ohm/cm

Figure 2 illustrates the image loops formed by joining the locations of the 16 points in image space when a dipole of unit strength exists at the 00 location The smallest loop is that calculated for the planar bounded medium The loop of intermediate size is that calculated for the spherically bounded medium The largest loop is that drawn from data that Frank determined experimentally in his torso model These same relative positions and sizes of the loops exist for media with these 3 boundary conditions in the subsequent figures All scales are in mv /ma cm

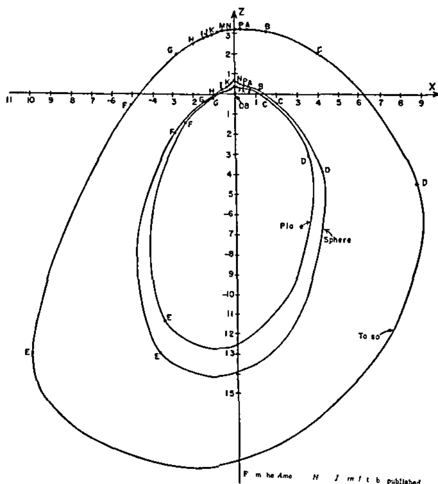


Figure 3

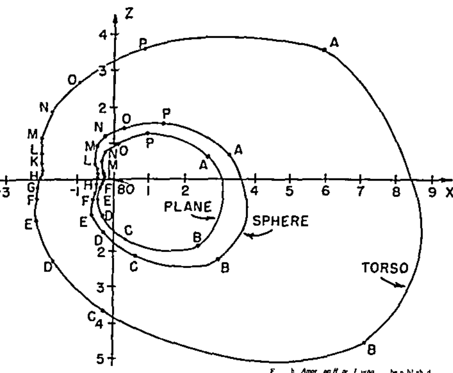


FIGURE 4

In FIGURE 3 the image loops are depicted for the 08 dipole FIGURE 4 illus rates these loops for the 80 dipole and FIGURE 5 for the 66 dipole This series f figures brings out two points that (1) the image loops vary both in size and ontour with different dipole locations, and that (2) for any given dipole loca ion the image loops vary in size depending upon the configuration of the miting boundary the contours of the loops however are similar regardless of he boundary

These qualitative observations have been studied quantitatively from a tatistical standpoint For each dipole location correlation coefficients be ween the x components of the 16 points A through P were determined for he following pairs of the 3 boundary configurations plane and sphere plane nd torso and sphere and torso In the same manner correlation coefficients ere determined for the z components In all instances the correlation coeffi ents were extremely high often 0 99 and never less than 0 96 Such results uggest that for a given dipole location the potentials calculated for a planar r spherically bounded medium could be utilized in a regression equation to redict rather accurately the potentials developed at analogous points on a orso model Analyses of covariance however indicated that the slopes of uch regression lines are influenced strongly by dipole location This finding gain emphasizes the fact that variations in dipole location are of the greatest

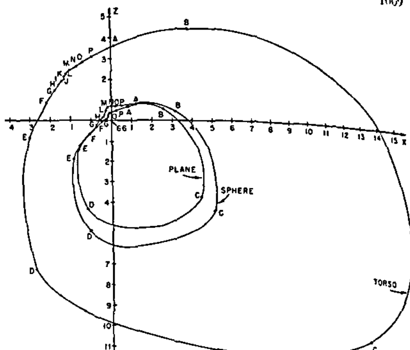


FIGURE 5

importance in the distribution of current in a volume conductor and that they take precedence over variations in the configuration of the boundary of the conductor

H H HECHT (*University of Utah Salt Lake City Utah*) In the discussion on homogeneity or inhomogeneity Nelson s remarks concerning the image problem perhaps have not been given sufficient attention Although Wilson Burger and Frank have more recently used the image concept perhaps others will go back to this problem of solving the annoyances of finite boundaries that with exceptions has been conveniently neglected in electrocardiography

The image analysis for the solution of boundary problems goes back to Lord Kelvin One of the most succinct discussions of the entire problem is given by Thompson who has written the biography of Kelvin[1]

Reference

1 THOMPSON P SILVANUS 1910 The Life of William Thomson 1 151 Macmillan London England (*Reprinted in* Circulation Research 1955 3 234)

H P SCHWAN (*University of Pennsylvania Philadelphia Pa*) I should like to comment regarding Katz and Burger s remarks Concerning Katz I do not

think that electrical impedances determined with direct current apply to electrocardiography any better than do impedances measured with low frequency alternating currents since the electrocardiograph frequency content extends from 1 cycle up to about 100 cycles with very strong components up to 20 cycles I do not think however that DC and AC resistance values of tissue that we have measured down to 5 cycles differ greatly Consequently while reading Burger s paper I wondered what could account for the discrepancy between his results obtained with direct current, and our results

First let me state some arguments in favor of our data The data we have given fit very well with any sound attempt to understand them theoretically Such an attempt may be based best on formulas given by Cole and H Fricke which are an extension of formulas originally given by Maxwell These formulas can be applied to blood as well as tissue if the proper form factors are incorporated In the case of the lung one must be careful not only to consider the air content of the lung but also the substantial blood content in lung If this is done the data we have obtained will make very good sense

Burger s blood and tissue data are quite different not only from our data but also from other published data Blood has been investigated thoroughly by many people Its electrical properties are very well understood Blood data that we measured are in line with results by others while Burger's values are too high On the other hand Burger s tissue resistance data in our opinion are too low Hence Burger gets a smaller difference between tissue and blood resistivity We get a ratio of about 10 to 1 while he gets a ratio of less than 2 to 1

Now let me comment about 4 electrode techniques such as used for example by Burger We also have experimented with 4 electrode systems Suppose we fill up a cylinder with a saline solution of a known conductivity and then apply 2 current electrodes at the cylinder s end caps and insert 2 pickup electrodes From a measurement of the potential across the pickup electrodes and the current passing the cylinder in principle we should obtain the impedance of the solution limited by the equipotential areas touching the pickup electrodes It is often thought that the use of this 4-electrode technique automatically eliminates any error due to electrode polarization since the pickup electrodes do not draw current A fraction of the current enters in the electrodes however and leaves it again even though the amplifier connected to the pickup electrodes has been provided with extremely high impedance (FIGURE 1) The moment this happens 2 polarization potentials are set up It is impossible to make the electrodes so perfect that these 2 polarization contributions cancel each other Consequently the electrode is lifted up by a differential polarization potential not only with DC but also with AC We have checked this effect by simply withdrawing our electrodes back deep in the wall of our cylinder thereby placing a large quantity of fluid in front of the electrodes and therefore making it difficult for the current to reach the electrode Indeed the more we draw the electrodes back the more perfect are the data In conclusion it is a misconception that 4 electrode systems automatically eliminate errors due to electrode polarization We wonder if this might explain some of Burger s results

Finally I should like to discuss some of the measurements that Burger carried out as a function of electrode distance Burger has made a study of the placement of electrodes and has shown that depending upon the placement different values are obtained for the specific resistance He starts for example in one series with values near 600 ohm cm and approaches finally 250 ohm cm depending upon how he has placed the electrodes Actually Burger s 600 ohm cm values compare well with our results while he favors the 250-ohm figure Could it not be that surface conductance in the skin and the presence of subcutaneous fatty tissue which is of very high resistivity cause this effect in part? Muscle tissue a good conductor is covered by subcutaneous fat a poor conductor and the electrodes are attached to the skin Therefore the

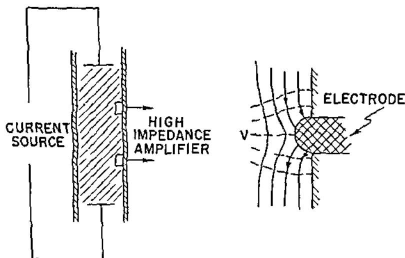


Figure 1

electrodes will not enforce a simple current distribution through all those conductors and one would anticipate that the result depended on electrode placement Under such complicated circumstance it seems difficult to derive, without further detailed analysis significant figures for the specific resistance from 4 terminal measurements on body segments as performed by Burger

C V Nelson (*University of Utah Salt Lake City Utah*) I do not think that the lack of smoothness of the potential-distribution curves could be caused by variations in the dipole moment of a single dipole These curves are all for given fixed instants of time Also a variation of dipole moment would cause only a uniform change in the strength of an entire field pattern With a single dipole one would get only one positive and one negative potential maximum on the thorax wall or even around a given horizontal level of the thorax

Measurements of the effects of inhomogeneous areas should certainly be extended to three dimensions

I was very interested to hear of Rijlant's work with an analog of a three dimensional infinite medium I have never come across anything like that before and I hope we shall hear more about it

In conclusion I think it is dangerous to make general statements in the field of electrocardiology Perhaps the fact that one group of workers finds only one effective dipole in the heart and that another group of equally able workers finds evidence of two or more dipoles may be explained by the fact that both groups are correct some of the time depending on experimental conditions

EXPERIMENTAL AND THEORETICAL ASPECTS OF VECTOR ANALYSIS IN ELECTROCARDIOGRAPHY

By G E Burch
Tulane University New Orleans La

The use of vector analysis in electrocardiography is not new Its application to theoretical experimental and clinical electrocardiography dating from the early days of Einthoven s and Mann s work has had considerable success and value its fundamental principles having been established many years before by mathematicians and physicists Application to electrocardiography was a logical result of its previous application to the study of electrical phenomena in space and in volume dielectrics and conductors Its usefulness in electrocardiography is evident It can be applied with extreme exactness to idealized systems or to models and the results obtained have conformed satisfactorily to well known predictions and expectations based upon mathematical and physical principles already known in other fields of science Without vector analysis the concept of the ventricular gradient would have been difficult to develop

Vector analysis first applied to frontal plane electrocardiography was soon used in three dimensional electrocardiography Recent interest in spatial vectorcardiography has increased the awareness of the applicability of vector analysis to electrocardiography Variations in the vector quantities in man are in accord with the general mathematical and physical concepts more easily observed for idealized systems the differences conform to well known electrical principles and errors are limited solely to the observations

Experiments with idealized systems should be continued in an effort to understand better the problems confronting the application of detailed vector analysis and vectorcardiography to man and other animals In the past most analyses have been qualitative and have usually been applied to a single plane The objective of further experimentation should be more accurate quantitative analysis of the scalar surface potential differences and the vector electric dipole or multipole characteristics associated with the activity of the heart of man with and without cardiac disease The main interest at present is directed toward examination of the electrical phenomena of cardiac origin quantitatively and three dimensionally Efforts have been directed to the heart as a whole for intact animals although it is known that an approach to the cells themselves would be of considerable if not greater value as shown by the relatively limited studies in experimental animals with the use of the capillary intracellular electrodes With much still to be learned from spatial vector analyses for the heart as a whole there remain unanswered many important problems that are more easily approached in intact man than by the local cellular approach to the bioelectric phenomena

For convenience in vector analyses in electrocardiography for intact

man many obviously inaccurate assumptions such as the following, have been made

(1) The electric activity of the heart may be represented as a single dipole or point source

(2) The body is an infinitely large volume conductor and electrodes placed upon certain points of the body may be considered to be remote from the dipole

(3) The body is a homogeneous volume conductor

(4) The heart is and remains centrally located in the body during its electric cycle

(5) The cardiac single electric dipole source the electrical homogeneity of the body the spatial orientation of the heart within the body the size of the body as a volume conductor and the central location of the electric source of the heart do not change significantly from man to man or from time to time within the same man in health or disease

(6) The locations of the electrodes on the body surface and of the electric dipole respectively define and are symmetrically located in a simple geometric configuration the spatial reference frame

That these assumptions are not without error has been as obvious to those who have made them as to those who have criticized them Nevertheless as applied to conventional electrocardiography they have served a useful theoretical and practical purpose even though they are as inaccurate in conventional electrocardiography as they are in spatial vectorcardiography Based on such assumptions conventional electrocardiography has nevertheless prospered and serves a useful purpose in clinical medicine It is extremely unlikely however that such a complex variable and nonidealized electrical system as the body of man can be studied electrocardiographically with complete vectorial exactness when only measurements on the body surface are permitted Major improvement may be possible but simple methods must and will prevail at least in clinical vector analysis even though there must be no limitations in theoretical and experimental vector analysis

Inaccurate assumptions and procedures obviously employed for convenience of thought must be subjected periodically to scrutiny and vigorous investigation regardless of their usefulness Examination of existing theoretical and applied principles of vector analysis in various phases of electrocardiography is currently of great interest to investigators the world over Nevertheless investigators should guard against encouraging too rapid adoption of new unestablished concepts and methods and they should avoid a premature discarding of existing useful ones This point is well exemplified by recent discussions and reports concerning reference systems and standardizing factors in electrocardiography and vectorcardiography Although there must be no limitations to experimental and theoretical vector analyses and methods there must be some restriction of the clinical applications Since man unfortunately is not an ideal electrical system from the standpoint of the investigators in electrocardiography and is so variable not only in disease but also in health it is the duty of those engaged in clinical research and clinical practice to accept changes and methods critically and cautiously particularly when the present approach, imperfect as it admittedly is has been so successful for so long

Surely the clinician must be practical, even though the investigator enviably may not need to be so limited

Obviously improvements in electrode placements should be welcomed if they offer definite advantages for general use The electrical distortions produced by the electrical inhomogeneities of the tissues of man the spatial orientation of the heart the finite characteristics of the body as a volume conductor and other factors may compensate for errors presumably demonstrated to exist from investigations with idealized systems and models The introduction of complex systems may discourage the use of vectorcardiography in man however whereas simple less accurate but satisfactory procedures might promote the more general application of vectorcardiography and might possibly demonstrate its clinical usefulness Such was the case for clinical electrocardiography

Therefore let us encourage more work by more investigators without restrictions on the methods of study and recording or in the application of vector analysis Let us remember that regardless of the observations in vector analysis in electrocardiography man himself is not an ideal electrical system and probably no single approach will be found soon that will be equally perfect for all men under any condition For the present a simple reliable and reproducible system of recording such as exists in conventional electrocardiography with careful and thoughtful analysis should prevail in the clinical application of vector analysis in preference to the complex time consuming methods that tend to shackle the use of the method clinically From the experimental point of view there should be no limitations whatever the investigator should permit his imagination and interest to dictate his methods and analyses without restriction

LEAD VECTOR PROJECTIONS I

By H C Burger

Department of Medical Physics Physical Laboratory of the University o Utrecht Utrecht The Netherlands

As a consequence of the electrical action of the heart there is a potential distribution on the surface of the body varying almost periodically with the heartbeat Our purpose is to acquire some information concerning this electrical action from this potential distribution It is only potential differences that occur in the laws of electricity never the potential itself and we are certain our information can make use of these differences

We know that the heart is often assumed to act like a single dipole (the heart vector) causing the electricity to flow in the trunk We know that this is an approximation for the dipole action is distributed over the heart muscle The vectorial sum of all these actions however can be considered as representing them if the heart is not too large There is no question of charges generated by the dipole as some investigators suppose The positive and negative charges in the conducting medium always occur in almost the same amount so there is no surplus of either or both charges We are not concerned with a problem of electrostatics but with a problem of electric current

The kind of dipole to be considered has been a point of some discussion Many say it is a current dipole whereas I am of the opinion that it is simpler to describe it as a voltage dipole It is not worthwhile to discuss this however since in both cases the potential distribution is not different The only difference is that the absolute value of the dipole deduced from measured voltages is different The ways in which it varies in magnitude and direction are found to be the same

Accepting the fact that we can describe the current field and potential distribution as generated by a single point shaped dipole we can deduce an algebraic relation between a voltage that is a lead and this dipole Although all of us are acquainted with this theory, I shall restate its essential points to serve as a basis for further explanation

A potential difference between two arbitrary points on the surface of the body depends on the momentary vectorial value of the dipole the heart vector The relation is a linear one that is the potential difference $V_P - V_Q$ between two arbitrary points P and Q is a sum of contributions of the three components X Y and Z of the heart vector H and each contribution is proportional to the corresponding component Thus generally for a heterogeneous body the following equation is true

$$V_P - V_Q = aX + bY + cZ \qquad (1)$$

The nomenclature used here is the same as that which van Milaan and I used in our first paper of 1946 [1] It is from this equation that the notion of the lead vector can be deduced It can be proved that the constant coefficients a b and c are components of a vector that more recently has rightly been called the lead vector The equation can be interpreted geometrically to indicate

that the lead $V_F - V_0$ is the so-called scalar product of the two vectors X Y Z = heart vector and a b c = lead vector The scalar product is the product of the projection of the heart vector on the lead vector multiplied by the absolute value (length of the arrow) of the latter (FIGURE 1)[2] This well known projection rule is a consequence of the above mentioned equation As it cannot be derived directly it is of secondary importance and is useful only as a convenient interpretation of the analytical result We shall not deal with the way in which the coefficients a b and c can be determined by experiments on a phantom[3] Frank has extended our earlier measurements for a great number of electrode positions and has been able to construct so many lead vectors that their combination gives us the image of the surface of the human body[4] From his lectures the meaning of this image should be clear

From three equations of the kind cited the three unknowns can be solved and so the heart vector (or dipole) X Y Z is found if the nine coefficients acb are known I shall not discuss the instrumental means used for this purpose

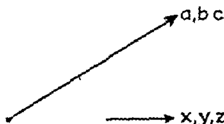


FIGURE 1 A lead is the product of the projection of the heart vector $\overrightarrow{H}$ on the vector $\overrightarrow{a\ b\ c}$ and the length of the latter

Such methods can give the vectorcardiogram that is the graphical representation of the heart vector as a function of time

To test the correctness of the assumption that the current field and potential distribution in the human trunk can be described as generated by a single dipole different ways can be followed

(1) The vectorcardiogram is recorded for two or more sets of electrode positions If the coefficients have the correct values and if the hypothesis of a single dipole has been made correctly the different systems as we may call them must give the same result that is the same vectorcardiogram This is much too optimistic however and in several subjects the agreement of the loops that must be identical appears to be rather poor[5] This could be attributed to the accepted values of the coefficients if this were the only cause of the disagreement there would have to be a simple relation between the curves (loops) that differ We should then be able to transform one loop into the other corresponding to another system by what we call a linear transformation This mathematical idea can be explained only by formula but it will suffice to say that in this case such simple operations as rotation or dilatation must transform one loop into the other In many cases the agreement is excellent and the average agreement for some systems can be made satisfactory if the

coefficients are chosen properly (FIGURE 2) This is possible even with uniform coefficients holding for all subjects Nevertheless there remain subjects that do not fit and cannot be made to fit by any choice of coefficients I therefore do not join the extreme optimists who claim that the description with a single dipole is correct within a few percentage points for all persons

It may be emphasized that I have arrived at this conclusion by examining many subjects normals as well as heart patients On the other hand the cases of bad correspondence constitute only a fraction of the total number so that I cannot agree with the opinion that correspondence is mere chance I am convinced that the potential distribution on the surface of the human body in first approximation can be described as caused by a dipole action of the heart—a single point shaped dipole As a consequence of this it must be possible to find a reasonable approximation of this dipole from the potential distribution that is from the recorded leads

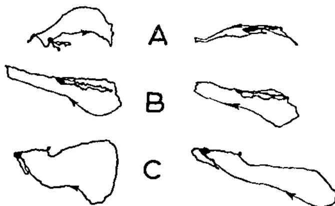


FIGURE 2 Estimation of the correspondence between different systems Figure 4 shows bad correspondence (mark 3) *B* very good correspondence (mark 9) and *C* sufficient correspondence (mark 6)

(2) The so-called cancellation or mirror pattern method devised and used by the Minnesota team leads to the same result[6,7] The easiest way to explain this method is to use the concept of the image space In this space the Wilson central terminal C is the center of gravity of the triangle LRF with corners in the images of L R and F If we draw a line through this point it intersects the image of the body surface in two mirror points M_1 and M_2 The potential differences M_1C and M_2C in the case of a point shaped dipole are given by the product of the projection of the heart vector $\overrightarrow{H}$ on M_1C and M_2C and the length of M_1C and M_2C respectively It is only this projection that varies during the heartbeat and the lengths M_1C and M_2C remain constant Therefore the ratio of the two leads M_1C and M_2C is constant and equal in absolute value to the ratio M_1C/M_2C The sign of these two leads is opposite as M_1C and M_2C have opposite directions

I shall not dwell upon the actual realization of this method and its use but I shall make some remarks in passing

(a) Instead of the central terminal any other point inside the image surface of the body can be used. In general we can connect an arbitrary number of electrodes by resistances that are high with respect to the skin resistance underneath each electrode. In image space this point is the center of gravity of the images of the electrode positions if the latter are given a weight inversely proportional to the corresponding resistance. In this way any point within the image of the body surface can be realized. The central terminal is not an important or special position among them.

(b) When the three points (images) of the two electrodes and the inside point are not chosen properly, that is, not on a straight line, the leads M_1C and M_2C in general do not show mirror patterns. There is an exception however, namely in the case when the heart vector changes during the heart beat in magnitude only and not in direction. The vectorcardiogram in this case is reduced to a line or to a very narrow loop. Then it is evident that all leads are proportional following the absolute value of the heart vector, that is, the length of the arrow as a function of time. There is no phase difference between the tops of the waves of the ECG and all leads differ in amplitude only. If the heart acts in this peculiar way, mirror points on the body surface cannot be found by looking for mirror patterns, for every pair of leads can give an exact cancellation. Reversely, it can be concluded that a wide loop makes it easy to find the mirror pattern position of a given electrode.

(3) The third method to test the hypothesis of the single dipole has been devised by Becking, to whom I am also indebted for the design of the vector cardiograph I have used for so many years. This method is a generalization of the mirror pattern method, but it has been devised independently. It can be explained algebraically or by geometrical means. I prefer the first method, but I shall not ignore the second.

From three equations of the same type as EQUATION 1 the three unknowns X, Y and Z components of the heart vector $\vec{H}$ can be resolved. Each component in the solution appears as a linear function of the three leads. Thus from three independent leads

$$
\begin{aligned}
V_1 &= a_1X + b_1Y + c_1Z \\
V_2 &= a_2X + b_2Y + c_2Z \\
V_3 &= a_3X + b_3Y + c_3Z
\end{aligned}
\qquad (2a)
$$

we deduce

$$
\begin{aligned}
X &= \alpha_1V_1 + \alpha_2V_2 + \alpha_3V_3 \\
Y &= \beta_1V_1 + \beta_2V_2 + \beta_3V_3 \\
Z &= \gamma_1V_1 + \gamma_2V_2 + \gamma_3V_3
\end{aligned}
\qquad (2b)
$$

The coefficients α, β and γ can be calculated from the set a, b and c according to the method of elementary algebra.

Now let us have a fourth lead V_4. This can be expressed in the components

of the heart vector in the common way

$$V_4 = a_4X + b_4Y + c_4Z$$

In this equation we can substitute the value of the three components X, Y and Z expressed in the three leads V_1, V_2 and V_3

$$V_4 = (a_4\alpha_1 + b_4\beta_1 + c_4\gamma_1)V_1 + (a_4\alpha_2 + b_4\beta_2 + c_4\gamma_2)V_2 + (a_4\alpha_3 + b_4\beta_3 + c_4\gamma_3)V_3 = p_1V_1 + p_2V_2 + p_3V_3 \quad (3)$$

So we see that for all phases of the heartbeat any lead V_4 is a linear function of the three other leads V_1, V_2 and V_3. From this relation we can deduce a very general test of the hypothesis of the single dipole. This could be done by cancellation, but I preferred to do it by a slightly different method. I have used the universal vectorcardiograph previously described.

The universal vectorcardiograph has four channels.[8] On one channel, let us call it 4, the lead V_4 is placed and made the spot of a cathode ray tube deflected horizontally. The other leads V_1, V_2 and V_3 are put on channels 1, 2 and 3 respectively. With the instrument it is possible to make a linear combination of V_1, V_2 and V_3, which means that they can be multiplied (amplified) by arbitrarily chosen factors p_1, p_2 and p_3, positive or negative. This linear combination is made to give a vertical deflection. On the screen a loop appears, more or less like a vectorcardiogram, but depending on these factors. By turning the knobs of the instrument this loop can be given all sorts of shapes depending on p_1, p_2 and p_3. If EQUATION 3 holds good, however, it must be possible to make the vertical deflection $p_1V_1 + p_2V_2 + p_3V_3$ equal to V_4—and this for all instants and, hence, for all phases of the heartbeat. The loop then degenerates into a straight line, making an angle of 45° with both horizontal and vertical direction (FIGURE 3). It must be possible to realize this independently of the position of the dipole, if only it is point shaped and fixed.

This method has been applied to a number of subjects.[9] I chose V_1, V_2 and V_3 as the three independent leads *LR*, *FR* and *BR* of the system B_1. These are the voltages between the left arm, left leg and chest electrodes respectively and the right arm was chosen as an arbitrary zero. As a rule, it was possible to reduce the loop to a fairly narrow and straight form, although it was never possible to make it so straight that the deviation from the ideal was imperceptible. In many cases the QRS loop could be made to fit quite well, but the T had a different direction. For some subjects the result was poor, without any indication as to the cause.

For the present I shall overlook the cases of bad correspondence and see what can be deduced from the coefficients p_1, p_2 and p_3 necessary to reduce the loop to a straight line under 45°. These coefficients obey EQUATION 3. From these equations we, therefore, conclude that

$$p_1 = a_4\alpha_1 + b_4\beta_1 + c_4\gamma_1$$

$$p_2 = \quad (4)$$

In this set of three equations p_1 p_2 and p_3 are evaluated by the procedure just explained When we consider the $\alpha\beta\gamma$ s derived from the abc s of system B_1 as known we see that from EQUATION 3 the three unknowns a_4 b_4 and c_4 can be solved This means that once it is accepted that a system of three leads is correct we can extend it by determining the coefficients of any additional electrode by the Becking method

For the group of subjects just mentioned the coefficients of a back electrode have been determined in the position as used in the system of the equilateral tetrahedron

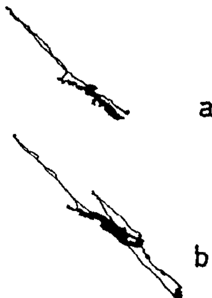


FIGURE 3 Method of Becking It has not been possible to reduce the movement of the spot to a straight line under 45 Figure a shows a normal beat and b shows a normal and a premature beat

Let us now switch over to the geometrical representation to display the results of these measurements In passing it may be remarked that the Becking method can be presented from the beginning in a geometrical way but to save time this will not be discussed

From a_4 b_4 and c_4 we find the position of the back electrode in the image space as these coefficients are its coordinates In FIGURE 4 the tetrahedron $RLFB$ is shown in frontal projection the horizontal one is omitted In these projections the positions of the back electrode are given each point giving the result for one subject At first sight these diagrams are rather disappointing The points are scattered over an area almost as large as the B_1 tetrahedron It must be borne in mind however that a previously mentioned circumstance plays a part Suppose that the vectorcardiogram of a subject shows a narrow straight loop so that it can be considered as a straight line Then all leads

follow the same time course, and they are proportional. As a consequence EQUATION 3 can be divided by this time function and EQUATION 4 does not follow from it. Therefore, there is only a linear relation between p_1, p_2 and p_3. There is an infinite number of combinations of dial positions p_1, p_2 and p_3 that reduce the loop to a straight line. The only restriction of the position of the fourth electrode in the image space is that it is situated in an experimentally determined plane. If the vectorcardiogram is not strictly a straight line but almost so, the definition of the point 4 in the image space is poor. The only thing we can say is that it lies in a disc shaped part of the image space. When the vectorcardiogram is more or less flat and its deviations from a plane are small, we have an analogous difficulty—we cannot decide where the image of the fourth electrode is situated in the image space. It may lie anywhere in a long, stretched region, thus explaining the wide scatter of points in FIGURE 4.

To show that this scattering does not mean that the single dipole hypothesis is inadequate, the following course was pursued. The center of gravity of all the points in the image space representing the back electrode was taken as the

FIGURE 4. Position of the back electrode in the image space in the frontal projection determined according to the method of Becking. Each cross indicates the result of the measurement on a single subject.

best position of this point It represented with the relative position of *LRF* omitting the chest electrode *B* the complete set of coefficients of the system of the irregular tetrahedron This system has the position of the electrodes on the body in common with the system of the regular tetrahedron but its coefficients are adapted to the human body The coefficients were founded on phantom measurements (B_1) as well as on measurements on the human body With these coefficients the components of the heart vector were calculated as a linear function of three independent leads between *L R F* and the back electrode and the vectorcardiograph was adjusted to this result The vector cardiograms were then recorded in a number of normal subjects and heart patients using the system of the irregular tetrahedron and these loops were compared with those of system B_1

The difference between these systems as to the position of the electrodes was that in the first there was an electrode on the back and in the second there was an electrode on the chest Comparison of the vectorcardiograms showed that the agreement was excellent in all cases for the frontal projections This however was self evident as the back and the precordial electrodes contributed very little to the frontal projection of the vectorcardiogram More signifi cant however was the fact that the agreement for the horizontal projections was satisfactory in most cases better than I have found between other systems Even the subjects for whom the image of the back electrode falls far from the average as rule gave good or reasonable results in comparing their vector cardiograms For the purpose of drawing practical conclusions from the vectorial behavior of the electrical heart action we can use one system or the other at will in the greater number of subjects

It cannot be denied however that the agreement is unsatisfactory in a fraction of all cases that cannot be neglected The true heart vector conceals itself behind phenomena we do not yet understand clearly Where are the e phenomena localized? We may get a hint of this localization by the study of vectorcardiograms of normal and premature beats in the same subject [10] Here nature itself performs an experiment in which the course of the excitation through the heart muscle is different in the two cases while the medium sur rounding the heart is the same If a bad correspondence between two systems of vectorcardiography is caused by a particular circumstance outside the heart—for example in the lungs—then we can expect that it would act in normal and premature beats as well and make their correspondence in differ ent systems bad Observation of vectorcardiograms in several subjects has shown however that there is no correlation between the degree of correspond ence between different systems in normal and premature beats In some the correspondence is good in normal beats and bad in premature beats and in others it is the reverse (FIGURE 5) So we must conclude that the cause of a bad correspondence very probably is localized very near the heart

A second question involves the problem of improving the experimental method to facilitate a more accurate and satisfactory evaluation of the total heart vector even in the unfavorable cases The way has been shown from two different sides Gabor and Nelson[11] proved that in a homogeneous con ductor bounded by an isolating medium the total dipole acting inside can be

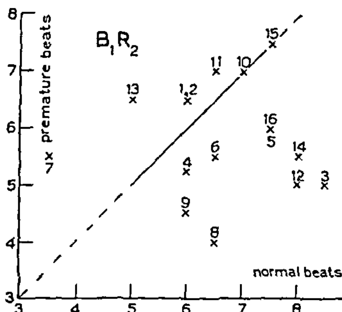


FIGURE 5 Similarity of the respective normal and premature beats in the systems B_1 and R_2

determined by a simple integration of the potential over the surface of the conductor Their surprisingly simple result cannot be put into practice exactly as an integral is the sum of an infinite number of infinitely small contributions Although we may not go as far as that it is clear that an improvement is possible by using more then four electrodes following the principle of the more the better McFee and Johnston[1] arrived at an analogous result They used the reciprocity theorem according to Helmholtz This theorem gives a relation between the potential distribution generated by a dipole in a conducting medium and the current field caused in the same medium by introducing a current in it by electrodes on its surface Their result is the same as that just mentioned—the total dipole action can be calculated from data over the whole surface of the body

According to these theories the components of the heart vector can be determined in practice as linear functions of a number of leads V_1 and V_2 There fore instead of EQUATION 2b we must express the components X Y and Z of the heart vector as the sum of a number (perhaps a rather large number) of terms each proportional to a lead Thus

$$X = \alpha_1 V_1 + \alpha_2 V_2 + \cdots + \alpha_n V_n \tag{5}$$

$$Y = \beta_1 V_1 + \cdots \quad etc$$

Now where should the electrodes be placed and what should be the values of the $3n$ coefficients? A decisive answer to this question should not be

expected I can only try to explain the method we employed to find an approximation

In clinical practice there is an advantage in the use of extremity leads as this method eliminates all uncertainty as to the position of the electrodes—the extremities themselves act as electrodes It is true that the left arm might be less suited as has been emphasized by Frank who has remarked that a little difference in the anatomical structure of the attachment of this arm to the trunk might give an *appreciable difference in the electrical situation* I thought it worthwhile to try the easiest method first however and used the extremities L R and F Apart from these we needed at least one more electrode but according to the reasoning expressed above I decided to use two more A back electrode and a precordial one were suited for example the back electrode used in the system of the (ir)regular tetrahedron and the precordial electrode of my system B_1

The precordial electrode has the drawback of being so close to the frontal part of the heart muscle that this area has more influence on the lead in which it takes part than other parts of the heart Therefore it is not the sum of all dipoles that works it is the nearer dipoles that weigh more heavily The reverse is true of the back electrode although in a lesser degree as it is not so near to the heart It might be wise to combine both systems to eliminate the errors just mentioned To put it as simply as possible we could take the average of the two systems that of the irregular tetrahedron and that with the *precordial electrode* (B_1)

To explain this with a numerical example let us calculate the lateral component X according to this averaging In arbitrary units we found from phantom measurements for B_1

$$X = 54LR + 16FR + 8BR \qquad (B_1)$$

$$(LR = V_L - V_R \quad etc)$$

In the system of the irregular tetrahedron the same component has been evaluated

$$X = 58LR + 16FR - 17B'R \qquad (\text{irr tetr})$$

Now we take the average of the two

$$X = 56LR + 16FR + 4PR - 8\tfrac{1}{2}B'R \qquad \frac{(B_1 + \text{irr tetr})}{2} \tag{6}$$

in which four leads occur We must use five electrodes L R F precordial and back *Instead of looking from one side at the heart* we now take into account the frontal view (B_1) and the back view (irr tetr) equally Applying the reciprocity theorem according to McFee and Johnston[1] [1] we could say that it is entirely impossible to realize a homogeneous sagittally directed current through the heart by using extremity electrodes combined with another electrode on the back or on the chest A combination of the latter two however combined with extremity electrodes could give a fairly homogeneous current It might be better however not to give the two systems an equal

LEAD VECTOR PROJECTIONS II DETERMINATION OF THE IMAGE SURFACE IN MAN

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Despite obvious difficulties and limitations as well as warnings and promising alternative methods such as those just presented by Burger it has been my feeling that a more direct approach to the determination of the image space in man should at least be attempted If feasible and successful such a method would overcome the several theoretical objections inherent in the application of the limited data obtained from models to living men with greatly varying positions and diseases of the heart and with greatly varying body constitutions Although all of the predictions of surface potentials based on Frank s model match exceedingly well the actual surface potentials measured on the subject used for construction of the model and support perfectly the theory of heart vector projection[2] on which the experiment was based nevertheless a certain amount of concern is inevitably felt by the clinical investigator if these data are to be applied with only quantitative modification to all patients with heart disease Generalizations are of course necessary and valuable in the conceptual stages of development of any branch of science A clinician deals with individuals however By sad experience he has learned that generalizations may frequently be not only inapplicable—they may be fatal In fact the whole purpose of all the research on quantitation of the effects of the conducting medium on cardiac potentials determined at the surface of the body has been to eliminate certain assumptions inherent in the Einthoven hypothesis and to give greater specificity to the electrocardiographic method All inclusive generalizations can defeat this purpose despite the precise nature of the individual experiment My desire therefore to design a method for the direct determination of transfer functions for surface leads in man can perhaps be understood Accordingly an experiment was executed by Jacob Hirsch and Stanley Briller of this department with the help of Nathan Marchand on the instrumentation involved

The study was undertaken to determine the shape of the tetrahedron that would be obtained if the 4 apices namely the right arm (R) left arm (L) left leg (F) and a point on the back 2 cm to the left of the 7th dorsal spine (B) were located upon the image surface A 47 cycle signal was amplified by means of a balanced constant current amplifier and passed through a selector switch to each of the 6 bipolar leads on the surface of the subject that comprise the 6 edges of the tetrahedron A special pickup containing 3 mutually perpendicular pairs of electrodes was placed in the esophagus approximately at the mid ventricular level This was used to detect the 3 orthogonal voltages developed in the esophagus as a result of currents introduced at the surface of the body Contrasted with the normal relationship between the heart generator and surface leads this arrangement will be recognized as an experimental interchange of generator and detector permitted by the Reciprocity

Theorem of Helmholtz[8] This was necessary in order to avoid thermal injury to the esophagus and possible undesirable cardiac effects

A second selector switch ganged to but shielded from the first made it possible to record each of the 3 components within the esophagus for each surface lead energized These were fed in turn through a cathode follower amplifier to 1 channel of a Sanborn Twin Beam Electrocardiograph (Model 62) A sharply tuned 47 cycle band pass filter was interposed at this point to remove 60 cycle pickup and the subject s esophageal electrocardiogram

The second channel of the recorder received a monitor signal directly from the generator This served as a phase reference for assigning polarity to the detected signals

The subject remained apneic in natural expiration for the duration of an experiment or about 40 seconds In some cases 20 mg of Nisentil hydrochloride* were given subcutaneously to facilitate the apneic period as well as to abolish the gag reflex at the time of passing the esophageal detector

It was found necessary to surround the esophageal pickup with a sleeve of cellophane This was filled with saline after introduction of the assembly into the esophagus This modification diminished fluctuations in the detected signal presumed to be due to poor contact with the esophageal wall Filling the sleeve from 50 to 100 per cent of its 100 ml capacity had a negligible effect upon the recorded signals

The magnitude of each of the 6 leads stimulated was obtained by taking the square root of the sum of the squares of the 3 orthogonal components For purposes of visualization lengths of copper wire were cut to scale and were soldered together at the ends in the proper positions to form tetrahedra The degree of closure of the sides of a tetrahedron was used as a test of the quality of each run Expressed as a percentage of the perimeter of the image tetrahedron the errors ranged from 6 8 to 15 8 per cent One set of observations in which gap in closure amounted to 37 per cent of the perimeter of the tetrahedron was excluded

Two normal male subjects were studied Subject 1 a 26-year-old male was 6 feet 1 inch tall and weighed 176 lbs Four sets of observations were made upon him after a single placement of the esophageal electrode Subject 2 was a 32 year old male 5 feet 10 inches tall weighing 175 lbs The esophageal detector was placed in him on 3 different occasions

FIGURE 1 shows in the frontal and left lateral projections the tetrahedra for subject 1 on the left and for subject 2 on the right Since the orientation of the orthogonally paired electrodes in the esophagus was unknown the spatial orientation of these image tetrahedra is likewise unknown It should be emphasized that lack of this information does not invalidate the shape of the tetrahedra obtained In the figure the frontal planes of the tetrahedra were assumed to be in and were drawn parallel to the plane of the paper

Each of these figures represents the average of all observations in each subject 4 in the first subject and 13 in the second For comparison the tetrahedra were constructed with the value of unity arbitrarily assigned to lead I

* Hoffmann La Roche Inc Nutley N J

It will be noted that in the frontal plane lead II is the largest in both subjects. In the left lateral projection lead BF is quite long in both and in subject 2 it is the longest of any of the leads. The difference in size of the 2 tetrahedra is also to be noted. Subject 1 was taller and of slenderer build than subject 2.

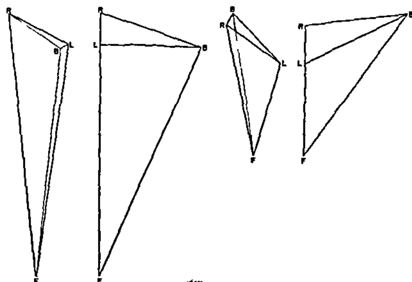


FIGURE 1

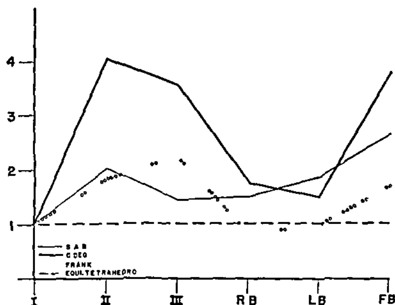


FIGURE 2

The reliability of the procedure was indicated by the range of repeated observations on each subject at each sitting These ranges were not excessive except in one set In all instances differences in values were probably caused by movement of the electrode caused by movement of the heart of the esophagus and possibly of the diaphragm Conceivably this variation could be reduced by simultaneous determination of all sides of the image tetrahedron In subject 2 studies on different days showed variations in values on each day These variations were probably ascribable to the inability to duplicate the exact location of the electrode from day to day

FIGURE 2 contrasts the results in subjects 1 and 2 with the values calculated from Frank s data obtained from a model of a human torso regarding lead I in each instance as unity Also plotted are the magnitudes of the edges of an equilateral tetrahedron which is obviously a straight line

It will be noted that in both subjects those leads that involve the back electrode as one pole of the lead have a magnitude greater than that of the corresponding leads calculated from the model On the frontal surface the comparative magnitudes of leads II and III are the reverse of what was found in the model These facts suggest that the electrode as used in these experiments was to the right of and posterior to the electrical center of the heart in Frank s model In addition in subject 1 it was probably also caudad to that point

In summary then we have described a technique that makes the determination of the shape of the image tetrahedron in man feasible The object of this presentation was to show that it can be done It is to be pointed out again that the orientation of the tetrahedron is unknown but that its shape is valid If our ideas on the relationship of the spatial areas of QRS and T should prove useful (see the presentation by Briller elsewhere in these pages) we shall not need orientation but only the lead coefficients

Obviously the esophageal electrode was not near the electrical center of the heart It is planned to conduct further experiments with a detector in the living heart Toward this end Briller has already constructed a three dimensional intracardiac electrode that looks workable

References

1 FRANK F 1955 Absolute quantitative comparison of instantaneous QRS equ potentials n a normal subject with dipole potentials on a homogeneous torso model Circulation Research 3 243

2 FRANK E 1954 General theory of heart vector projection Ci culation Research 2 258

3 HELMHOLTZ H 1853 Über einige Gesetze der Vertheilung elektrischer Strome in Korperlichen Leitern mit Anwendung auf die thierischelektrischen Versuche Ann Physiol Chem 29(3) 227

LEAD VECTORS AND TRANSFER IMPEDANCE*

By Otto H Schmitt

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Biophysical theory and the technology of instrumentation have advanced so far during the last few years that we have only ourselves to blame if we are still unable to agree qualitatively and indeed semiquantitatively upon the relationship between the heart as a generator of action currents and the potential differences arising at the surface of the body as a result of these currents We are not yet prepared to understand fully the detailed physiological implications of the potentials that we measure but we should be able to unscramble adequately the relationship between the potentials measured at the body surface and the potentials that would be measured were we able to suspend the heart in a geometrically simple container filled with uniformly conducting fluid

We cannot yet escape the empiricism implicit in our interpretation of cardiac events in terms of electrocardiographic data so there is room here for differences in clinical interpretation based upon extensive personal experience and intuitive understanding However all correct theoretical reconstructions should lead to the same heart generator for a given set of surface potentials One theoretical treatment might be much simpler or more easily understood intuitively and another might involve measurements that are especially easy to make but all should be mutually consistent

It is the purpose of this study to provide theoretical and technical means for testing objectively the degree of consistency between the several popular electrocardiographic recording systems and incidentally to provide a mental tool for easy understanding of the universal relationship between measured potential and active source independent of the peculiarities of a particular lead system used in any specific study This tool is transfer impedance

Transfer impedance bears a simple mathematical relationship to the lead field vector that has been utilized in some other theoretical developments It is much more easily understood intuitively however being defined directly in terms of an action current source and the accompanying measured potential Lead field concept starts with the notion of an externally applied current and measures the electric field in the source region relying upon a reciprocity theorem to guarantee that source and measurement positions can be interchanged provided careful attention is paid to the specification of source and measuring impedance dimensions and proper conversions between field and potential differences

Let us start with the idea of a small bundle of active muscle fibers producing an action current somewhere in the heart and a pair of electrodes picking up a resultant action potential somewhere at the body surface (or if preferred at internal points) As long as the surrounding tissue is electrically linear

* The research reported in this paper is supported in part by research grants from the National Institutes of Health Bethesda Md from the Minnesota Heart Association St Paul Minn and by a research contract with the Office of Naval Research Washington D C

this recorded action potential will have a constant ratio to the action current generated by the muscle bundle (1) whether the surrounding tissue is homogeneous (2) whether it is anisotropic, (3) whether the recording point is nearby or distant and (4) whether the generator itself is linear or even if it has a strong rectification characteristic The universality of this constant relationship makes the ratio one of great interest and utility

Notice that the ratio is that of a voltage to a current This makes the name impedance appropriate for according to the general form of Ohm s law impedance $Z = E/I$ and because voltage difference is produced at points other than those at which current is introduced transfer rather than simple impedance is implied This usage is consistent with conventional four terminal electrical theory where the concept of transfer impedance is well known Were we not playing safe and anticipating the eventual question of some small frequency dependence and phase shift transfer resistance and not transfer impedance would be used

To make the notion of transfer impedance physiologically useful we must make provision for two features distributed sources and varying orientation of sources This we do by making transfer impedance what is called a vector point function and by resolving physiological sources into distributions of current dipole sources Physiological action current sources are always intrinsically bipolar in nature for only when current leaves a cell somewhere and enters elsewhere in almost exactly equal amounts does a measurable action potential develop externally In a fiber type cell such as nerve or muscle significant action current is generally developed only along the length and the externally measured potential will be found proportional not only to the magnitude and sign of the current but also to the distance between points of entrance and exit of the current from the cell It now becomes apparent why we must use current dipole moment which is the product of current with the distance between entrance and exit points of current rather than current itself in computing transfer impedance and also why action currents usually correspond in direction to tissue fiber direction

Technically we should always think of a finite dipole source such as a muscle fiber as made up of an infinite series of infinitesimal true dipoles arranged linearly between entrance and exit points but this is generally only of academic importance except when microelectrodes are being used

Notice that scrupulous attention is being given to the concept of the cells as current sources not as voltage sources As pointed out elsewhere dipole or finite dipole current sources are linearly summable while voltage sources are not Notice also that nothing has been said that would limit the proportionality of response to sources oriented in any particular direction Transfer impedance is completely general in this respect

Potential developed at some pair of electrodes is not of course insensitive to orientation of current sources in fact it is the simple predictable relationship between the dipole source orientation and the measured potential that makes it so useful Consider a tiny current dipole ource of moment M at some position within the body causing a potential to be picked up at external electrodes P Some dipole orientation in space defined by two angles θ and ϕ

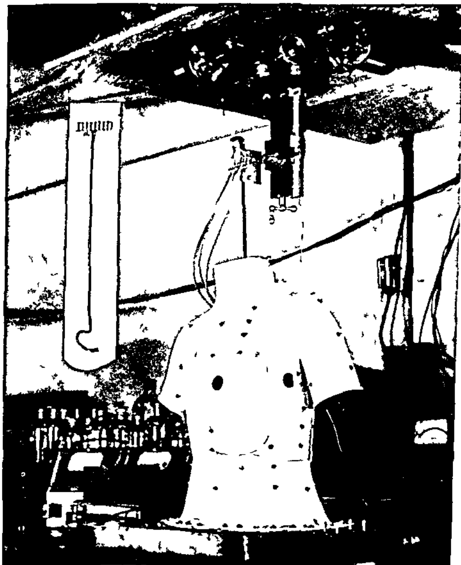


FIGURE 1 Plastic torso model with triple dipole source and servomotor-driven three dimensional scanning system From Schmitt and Simonson *American Medical Association Archives of Internal Medicine* November 1955

In the standard transfer impedance mapping procedure a lead system is chosen for testing and is applied to the model Signals from the leads are recorded by vacuum tube voltmeters for a group of 9 source dipole positions at the corners and center of a cube with a volume of 8 cu in surrounding the heart center Inch dimensions are used because metric lead screws are difficult

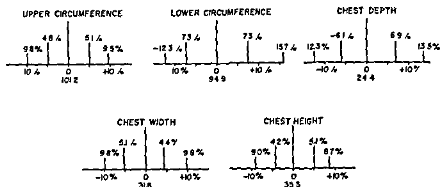


Figure 2 Distribution of torso types of 275 normal men The dimensions are in centimeters the ranges are in percentage from the median for groups of 10 25 50 75 and 90 percentile

to obtain. Practically speaking the cube can be regarded as 5 cm on an edge For each dipole source position signal in the lead is recorded separately for horizontal vertical and sagittal excitation so that 27 transfer impedance values are obtained for each lead component For a typical orthogonal lead set such the cube system 81 values are needed Values of Z_{tx} Z_{ty} and Z_{tz}, the Cartesian components of Z_t for a particular lead and dipole source position are then added vectorally to give one Z_t value expressed as a strength and a direction for that particular source position This process is repeated at successive positions Eventually a space scale model is made that quickly shows the over all pattern of Z_t for the lead

Representative stereophotographs of a highly corrected orthogonal composite lead system (SVEC III) a badly nonuniform spatial system (cube system) and the highly contorted precordial system are included in FIGURE 4 Experienced stereo viewers will be able to examine these pictures directly but

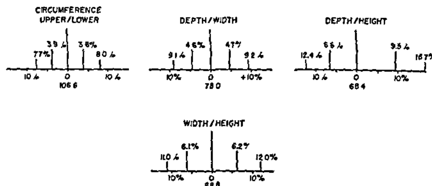
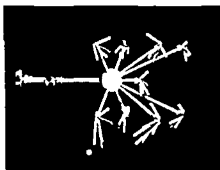
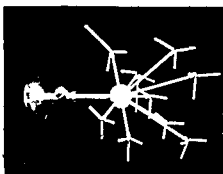
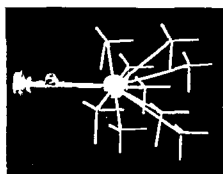
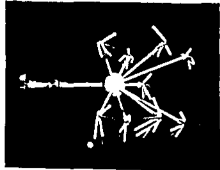


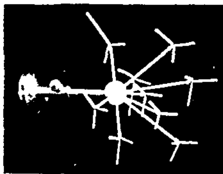
Figure 3 Distribution of torso types of 275 normal men The dimensions are in centimeters the ranges are in percentage from the median for groups of 10 25 50 75 and 90 percentile


Precordial Leads
V_1 V_2 V_3 V_4 V_5 V_6


Duchosal – Sulzer
Cube System


SVEC III Lead System





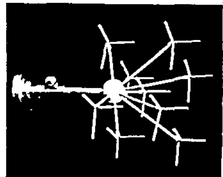


FIGURE 4

the use of a standard stereo reader will make visualization easier and more exact

The development of highly corrected lead systems is accomplished by calculating spatial partial derivatives of transfer impedance and then juggling these coefficients to nullify unwanted components and to preserve desired components and keep them constant This procedure for one set of partials entering into the development of the SVEC III Z lead is shown in FIGURE 5

In appraising the over all desirability of a lead throughout the heart region attention must be paid not only to the average direction and average strength of a lead but also to its absolute direction and its variability both in strength and direction reckoned absolutely and relatively A lead that is uniformly skewed in one direction but is constant in strength is not necessarily bad while one nearly ideal in direction with a few very weak or strong points may be far from desirable How can a simple index of uniformity be derived?

We have chosen to represent the mean direction of a transfer impedance vector for a specified lead as the direction taken by a vector made up by summing vectorially all 9 constituent vectors and have chosen to represent its strength as the normalized strength of this composite vector The variability is measured by the root mean square standard deviation measured with respect to this composite normalized vector so that very large single aberrations will impose a relatively severe penalty Angular variability is evaluated by the angular standard deviations from the mean direction and from the ideal direction In TABLES 1 and 2 data are summarized for a variety of conventional and newly developed lead systems TABLE 3 shows a sample complete set of data as *derived from the model system for the precordial lead* V_1 These data permit one to decide whether the summarized index represents realistically the performance of a lead

While the homogeneous-model method is not ideal for testing lead systems it probably forms a fairer more objective appraisal than is otherwise available Consequently this laboratory is prepared within its limited facilities of time and personnel to test and evaluate lead systems proposed in other laboratories

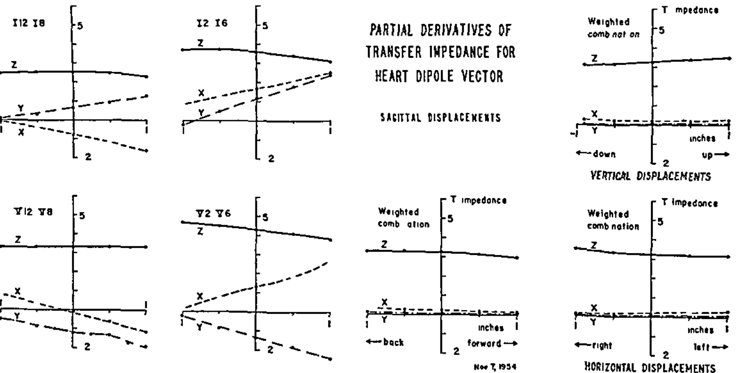
The model technique is not limited in its utility merely to the testing of proposed or existent leads it is capable of performing an important synthetic

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FIGURE 4 Strength and direction of transfer impedance vectors in several lead systems for sources within the heart region as reconstructed from homogeneous model measurements. In each lead system the components of transfer impedance are measured at each of nine representative points within the normal heart region (at the center and corners of a cube 2 in. on an edge) At each point the resultant value of Z for a lead is plotted vectorially as a bar whose length measures the sensitivity of the lead to activity in that region and whose direction indicates the direction in which current must be generated to be recorded maximally in that lead Vectors of a particular lead can be identified by their general direction which approximates the theoretically expected direction and by their color coding which is the same throughout each picture In each case the model is viewed from in front of the subject

The stereoscopic photographs are best viewed by a standard 5-in focal length stereo map reader but may with a little practice be seen without optical aids by bringing them close to the eyes until the pictures fuse into a single blurred image and then moving them away slowly until focusing can be achieved meanwhile disregarding the two outer images that appear Cross eyed viewing will result in a pseudostereo image with the *sagittal axis reversed* and hence must be avoided

From Schmitt and Simonson *American Medical Association Archives of Internal Medicine* November 1955



PARTIAL DERIVATIVES OF
TRANSFER IMPEDANCE FOR
HEART DIPOLE VECTOR
SAGITTAL DISPLACEMENTS
I12 I8
I2 I6
V12 V8
V2 V6
Weighted
T impedance
inches
← down
up →
VERTICAL DISPLACEMENTS
← back
forward →
Nov 7, 1954
← right
left →
HORIZONTAL DISPLACEMENTS

FIGURE 5

function One of the commonest questions we face is that of reconstructing the dipolar source that might conceivably give rise to an experimentally measured set of electrocardiograms Several years ago in connection with our mirror pattern cancellation studies my associates and I pointed out the danger inherent in neglecting the time phase factor in reconstructing spatial central dipoles from constituent leads The problem is further complicated if we try to take into consideration the variability of transfer impedance for nonuniform leads

It is manifestly unrealistic to insist that potentials measured with a lead system of varying transfer impedance be represented by a concentrated dipole at a specified place but this formalization is prominent in much of the thinking in the field and consequently it is important whether valid or not It is formally true that so long as we limit our data to those obtained from three approximately orthogonal leads and refuse to acknowledge any inconsistencies observed via other leads we can often represent all of the complexes of a spatial VCG exactly by an appropriately manipulated dipole fixed in position even though that position be chosen rather carelessly

From study of the theory of multiple feedback networks it turns out that the model method can be made to synthesize automatically the orthogonal dipole components required for a concentrated source at a specified position in order to develop a measured set of near orthogonal potentials even though the proposed electrode system is of unknown transfer impedance or is highly irregular

Experimentally the model is fitted with whatever electrode system is to be applied to the patient and these electrodes are strongly fed back via an amplifier to the dipole within the model Signals from the human subject are then injected appropriately into the loop and the dipole excitation is either read on a conventional recorder or is viewed spatially on the SVEC instrument

Should there be no solution to the problem the system will usually become unstable but if there is a reasonably possible solution it will be calculated instantly and presented at once as the Cartesian components of the excitation required The system has only recently been constructed and cannot yet be reported on in detail beyond an affirmation of its adherence to theory in simple test cases

If we believe the theory and experimental evidence of the preceding para

FIGURE 5 Development of uniformly orthogonal leads by weighted combination of electrode potentials as guided by measurement of spatial partial derivatives of transfer impedance For each constituent lead expected to form part of a weighted orthogonalized lead combination variation of transfer impedance is measured as the source dipole scans throughout the heart volume Scans are made once successively in all three primary directions with each principal dipole direction excited In general the principal or desired component (sagittal or Z in the case illustrated) will dominate in a useful lead constituent but will vary in strength while the two undesirable or contaminating components will be small but finite and will also vary in strength and possibly in sign By judicious weighting and combining of constituent leads a composite lead is eventually found in which contamination components nearly cancel for all regions within the heart and for which the desired component remains strong and nearly constant One electrode may form part of more than one constituent lead and because proximity effects are canceled rather than evaded electrodes close to the heart may be used with the result that large easily measured potentials are obtained

From Schmitt and Simonson *American Medical Association Archives of Internal Medicine* November 1955

Table 1
Relative Transfer Impedance of Common Electrocardiographic Leads

Lead	Strength	Percent S.D.	Mean φ degrees	Mean θ degrees	Angular S.D. degrees	
					From mean	From ideal
I	1.08	20.4	98.3 (90)	14.8 (0)	10.3	20.1
II	1.16	12.3	89.5 (90)	−63.0 (−60)	6.8	7.6
III	1.44	14.2	272.2 (270)	−67.5 (−60)	7.9	14.1
aV_L	1.16	18.8	91.4 (90)	47.7 (30)	9.4	22.3
aV_R	0.86	14.8	270.3 (270)	25.9 (30)	10.1	11.5
aV_F	1.17	11.5	2.7	−84.1 (−90)	6.8	9.1
V_1	1.19	46.0	334.0	22.2	26.6	
V_2	1.40	47.2	12.0	22.3	25.0	
V_3	1.42	52.6	34.2	9.5	26.0	
V_4	1.21	48.4	45.0	−2.0	26.7	
V_5	1.09	47.8	67.7	−1.4	27.7	
V_6	0.91	27.9	95.6	3.7	28.1	

Table 2
Relative Transfer Impedance of Orthogonal Lead Systems

Lead	Strength	Percent S.D.	Mean φ degrees	Mean θ degrees	Angular S.D. degrees	
					From mean	From ideal
Duchosal Sulzer						
X	0.81	40.7	113.4 (90)	−11.0 (0)	19.2	30.6
Y	0.78	22.6	34.5	76.5 (90)	12.1	17.5
Z	0.76	44.3	354.8 (0)	−16.3 (0)	19.5	25.8
Wilson Burch						
X	1.14	20.3	98.2 (90)	15.4 (0)	10.0	19.9
Y	1.20	17.4	186.2	59.7 (90)	10.8	32.3
Z	0.60	39.0	6.7 (0)	−27.2 (0)	16.9	35.5
E Frank						
X	1.12	15.2	86.8 (90)	2.1 (0)	8.9	9.8
Y	1.16	6.9	3.4	85.0 (90)	5.6	7.5
Z	1.09	16.5	358.0 (0)	−8.8 (0)	9.7	16.5
SVEC II						
X	1.64	22.9	84.8 (90)	−4.2 (0)	11.2	13.0
Y	1.41	3.0	216.8	86.4 (90)	1.5	3.9
Z	1.33	31.6	354.0 (0)	−8.5 (0)	15.1	18.5
SVEC III						
X	1.33	10.2	90.1 (90)	3.6 (0)	5.8	6.8
Y	1.41	3.0	216.8	86.4 (90)	1.5	3.9
Z	1.00	4.0	359.9 (0)	−1.0 (0)	2.3	2.5

graphs it becomes obvious that we must consider seriously the introduction of composite leads into conventional clinical electrocardiography. This immediately raises a host of new questions. Must we have very elaborate electronic systems of many channels to accept all the lead data? Can we use resistive combination networks? Is it prohibitively difficult to apply the rather formi

TABLE 3
SAMPLE OF COMPLETE DATA FROM WHICH CONDENSED DATA OF TABLES 1 AND 2 ARE DERIVED
This Sheet Refers to the V_1 Lead

Dipole position			Component excited			Strength r	Azimuth φ	Elevation θ
	y			y				
1	1	−1	0.23	−0.39	1.04	1.14	[illegible]	−20
1	1	1	1.18	−0.88	2.42	2.83	26	−19
−1	1	1	1.07	−0.33	0.78	1.36	54	−14
−1	1	−1	0.53	0.43	0.48	0.84	48	31
1	−1	−1	0.36	0.12	0.99	1.06	20	7
1	−1	1	1.26	1.42	2.10	2.83	31	30
−1	−1	1	1.06	[illegible]	0.68	1.62	57	39
−1	−1	−1	0.51	0.06	0.54	0.75	43	5
0	0	0	0.87	0.66	1.01	1.49	41	26

dable arrays of electrodes required by a system such as SVEC III or must we settle for a reasonably good system such as the E Frank system even though it is not adequately compensated for vertical distributions?

We must make a hard choice between quite different advantages and disadvantages in deciding whether to use resistance networks to combine components before the amplifiers or to amplify and then combine. There is no question whatsoever that combination after amplification is theoretically more desirable if the instrumentation cost is not too high. With the SVEC system seven push pull inputs would be desirable instead of three sets. Clearly this is too high a price to pay unless amplifiers are very cheap or funds freely available. In this system there is almost no attenuation penalty for premixing so that one unquestionably uses a three channel amplifier after a mixing network.

If the anticipated trend toward transistorized amplifiers continues however in the interest of reduced noise we may see amplification before mixing. Good transistor amplifiers are strange to one accustomed to vacuum tubes in that they may present an input impedance of nearly a megohm yet increase their output noise sharply when fed from 50 000 ohms instead of 5 000. With this noise penalty for high input impedance we are compelled either to amplify before mixing or to mix in very low impedance networks.

Transistor amplifiers consume so little power and are so simple that multiplying their number is not too forbidding. There is also a hidden danger in resorting to low resistence networks that should not be ignored even by those of us using conventional tube electrocardiographs with low impedance central terminals. The resistance of an ordinary electrode connection to the skin prepared in the usual way by a reasonably conscientious technician with electrode paste and a little rubbing is higher than many of us are prepared to believe without documentary evidence. FIGURE 6 shows the distributon of impedance found for 87 electrodes applied to the wrists and ankles of 30 individuals the values are those for each individual electrode not for the pair. It is evident that we must admit 2500 to 3000 ohms as common and so must use mixing networks of at least 25 000 and preferably 100 000 ohms if we are to swamp this error.

The problem of applying multiple electrode arrays to permit good lead compensation has in our opinion been grossly exaggerated It is possible that one can waste as much as 20 min sorting out 15 wires and attaching them to electrodes each individually pasted and located on one strap or another, and then getting the patient into a resting position with all this hardware attached It has been our experience however that an electrode jacket with all electrodes in place but individually movable without disconnection can be fitted to a subject in 2 min or less Tests currently in progress require that such an electrode vest (FIGURE 7) containing not only the SVEC III electrodes but V_1 to V_6 and several others as well, totalling 21 be fitted onto subjects run in quick succession in a mass measurement schedule With a team of 2 persons to fit the electrodes and make recordings it has been possible to keep a 10 min schedule continuously, taking 16 recorded leads on each subject having ample time to record several items identifying the subject and wash off electrode paste and so forth Possible application of nonpasted electrodes lends hope that this procedure may be simplified even further

With this favorable experience in the use of multiple specifically arrayed electrodes we have little patience with the current search for rough approximations to distributed electrodes Large metal electrodes faced with conductive paste or electrolyte allow skin impedance variations to play too large a role Large electrodes of sponge or felt change their weighting too much with variation in wetting and attachment Even the moderate price in distortion paid to eliminate 4 or 5 electrodes and to locate all the torso electrodes on one belt seems uneconomical especially if one takes into account the more careful belt adjustment required with such systems

Granted that highly corrected leads can be established and that they can be used clinically without too much inconvenience do they offer any theoretical or practical advantage? It seems probable that they will yield both On the theoretical side it is always advantageous if experimental data can be brought into closer correspondence with the concepts in terms of which they are to be interpreted On the practical side it becomes a simple matter to transform data from one orthogonal scheme into another with the turning of two knobs and without moving any electrodes a simple resolver will give *any* possible uniform lead Three lead data recorded on magnetic tape can be played back



FIGURE 6 Distribution of limb lead impedances found for 87 electrodes applied to the wrists and ankles of 30 different individuals The impedance is in magnitude ohms (60 c/s) and is calculated for each limb impedance separately not for the entire lead circuit The ordinate is frequency of occurrence the abscissa impedance in ohms



FIGURE 7 Adjustable elastic vest which permits quick and convenient attachment of complex lead system electrodes to the patient All electrodes are attached to the vest so that they can be put on in a single motion but each electrode may be positioned or replaced individually The cable of leads from the vest terminates in a quick disconnect plug so that the patient need not be brought to the recorder before the vest is put on and so that alternative lead vests can be kept clean and on hand The vest illustrated provides for the 14-electrode SVEC III system the 6-lead precordial set and for conventional limb leads

for recording on any time base or vector recorder or for spatial vector display The recordings need not be in the original leads but can be reoriented at will This freedom of spatial resolution is possible because fully orthogonal data are invariant for such transformations Above all this re resolution theoretically permits automatic systematic correction for heart positions and so can presumably put all displays on a common orientation basis aligned anatomically with the heart rather than with the body

Lest we be carried away with enthusiasm for the seemingly precise analysis that transfer impedance theory yields it now seems appropriate to introduce some experimental data that compel us to go cautiously and to re examine each piece of evidence carefully These are some data measured in our laboratory recently and strongly supported by additional experiments done by E Simonson and some of our associates

If we accept the old notion that the several presumably orthogonal lead systems derived from such forms as cubes and tetrahedra are more or less

TABLE 4
QRS AND T AXES IN VARIOUS ORTHOGONAL LEAD SYSTEMS

Lead system	QRS			T			ΔA
	Az	El	Ampl mv	Az	El	Ampl mv	
Duchosal Sulzer	94	−67	0.8	65	−65	0.2	17
Grishman	92	−50	1.0	80	−49	0.3	8
Wilson Burch	89	−89	0.95	68	−50	0.4	39
Briller	6	−72	0.9	84	−40	0.3	49
E Frank	83	−55	1.05	63	−46	0.3	15
SVEC II ab	76	−89	1.75	65	−60	0.4	29
SVEC III	101	−63	1.3	63	−43	0.4	30
E Simonson	122	−80	1.45				

All measurements made on the same normal individual

equivalent differing perhaps slightly in strength of components and detaile variation but basically alike then we should expect that an individual woul give reasonably similar spatial patterns in any of these systems We trie this, using the SVEC II display system which allows immediate direct mea urement of spatial orientation shape, and magnitude of the several complexe We were not too surprised to see the differences tabulated in TABLE 4 Carefi choice of the test subject and a comparison of several individuals verified th fact that these were not freak results A comparison of repeat measuremen on one individual using two observers proved that the discrepancy was not i the measurements (TABLE 5) As a further check the measurements wei repeated at intervals over several days the electrodes being repeatedly re moved and applied still with consistent results (TABLE 6)

Evidently there is serious but not violent distortion in the relationship c

TABLE 5
REPRODUCIBILITY OF INSTRUMENTAL MEASUREMENTS SVEC METHOD
The Values are Average Angles in Degrees Plus or Minus Mean Deviations

Observer	Number of Readings	QRS		T	
		Azimuth	Elevation	Azimuth	Elevation
J D	7	102 ± 2.0	−40 ± 0.8	60 ± 2.5	−30 ± 1.6
R L	7	99 ± 0.9	−40 ± 0.8	59 ± 2.4	−29 ± 1.6

TABLE 6
SHORT TERM VARIABILITY OF SVEC MEASUREMENTS
The Values are Averaged for 7 Measurements over 50 Days Plus or Minus Mean Deviatior

QRS			T		
Azimuth	Elevation	Amplitude mv	Azimuth	Elevation	Amplitude mv
104 ± 3.8	−39 ± 1.3	3.0 ± 0.05	62 ± 5.0	−30 ± 1.5	0.9 ± 0.10

one system to another and the systems do not merely rotate or stretch the data for this would not lead to such differences in the pattern of behavior of T with respect to QRS Additionally it seemed evident that the spatial pattern shape was differentially changed in detail

On the basis of these facts we reasoned that if these were indeed moderate distortions brought about by detailed differences in the transfer impedance pattern slight reorientations of the heart could result only in practically identical *changes* in the resulting patterns As a test of this hypothesis the subject was asked to inhale and exhale almost maximally and the experiment was repeated in each position We were amazed to see that the resultant large angular shifts were not even consistent in sign in the several systems and that the T did not particularly follow the QRS Obviously something more than a simple rotation of coordinates was involved

It was reassuring to see that the systems that had turned out best in the model measurements were most similar in response and showed less aberration The residual shift is real however and cautions us to be alert for inhomogeneity effects in future analyses

It is inappropriate to close this discussion without introducing the topic of absolute as against relative specification of transfer impedances From our earlier discussion of transfer impedance it is obvious that the voltage measured at any lead must among other things depend upon the resistivity as well as upon the shape of the body Were the dipolar source and leads left fixed and were the body resistivity doubled then the measured voltage would double for a source of specified dipole current moment

If the model measurements of transfer impedance had been absolute rather than relative and if the mean resistivity of the human torso were known we could then specify electrocardiographically measured potentials in actual milliampere centimeters of heart dipole moment and thus come much closer to the ideal with which we started namely specification of heart current production in physiologically meaningful terms

Realization of the ideal of absolute tran fer impedance measurement requires two hitherto unavailable items of data the mean resistivity of the human torso accurately established on a group sufficiently large to permit statistical specifications and the absolute calibration of the dipoles used in model work

The solution of this last problem is straightforward but not particularly easy Because of the awkward boundary conditions to be met it is not feasible to calculate the moment of a triple dipole made up as a cube with somewhat shielded faces Consequently a direct calibration is substituted For this purpose a standard simple dipole of easily calculable moment was introduced into a 30 in internally insulated saline filled sphere (FIGURE 8) and the resultant field was measured The unknown dipole was then substituted and by direct comparison was calibrated and checked for symmetry

Measurement of human torso resistivity is more difficult but will be undertaken on a statistically meaningful basis shortly In a token sample of measurements made by passing alternating current from a constant current source through the subject from head to foot and then measuring the potential gradient

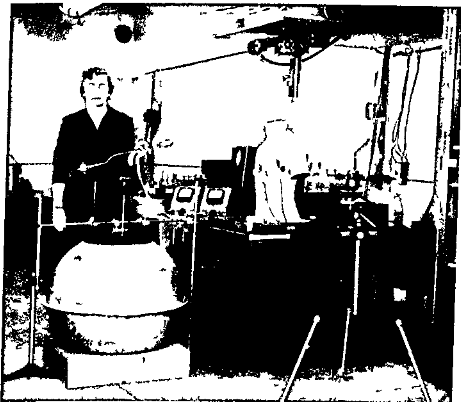


FIGURE 8 System for absolute calibration of transfer impedance measurements The triple dipole source is accurately orthogonal and can be precisely located and oriented in the model but because of its complicated form which makes direct calculation prohibitively difficult it must be calibrated in terms of a simple dipole The direct comparison of dipole sources is carried out in the 30 in insulated sphere which is filled with saline of controlled conductivity

TABLE 7
TRANSFER IMPEDANCE OF COMMON ELECTROCARDIOGRAPHIC LEADS

L d	Str gth hms-cm
I	0 47
II	0 51
III	0 63
V_1	0 52
V_2	0 61
V_3	0 62
V	0 53
V	0 48
V_6	0 40
SVEC III	
X	0 58
Y	0 62
Z	0 47

on the chest and on the back in the heart region it has been possible to obtain reasonably reliable approximations of the desired resistivity Typical values of ρ were 450 ohms cm but these data must be regarded as only tentative *

Utilizing this value of ρ and the absolute transfer impedances for the model it has been possible to arrive at sample values for the transfer impedance of a few common leads These values are presented in TABLE 7 from which we see that Z_t for all useful leads will be of the order of half an ohm per centimeter Human heart action currents must then typically involve about one half milli ampere centimeter of dipole moment This quantity is conveniently remem bered and is perhaps more than we should have expected in view of the great internal cancellation ordinarily involved in the normal beat

We must not hope to be able to reconstruct the heart action current distribu tion in detail from the externally measured potentials but it now appears that we can hope to specify its absolute magnitude and to obtain properly inte grated spatial representations of its temporal activity with good accuracy in the not too distant future

* Statistical measurement of a group of 203 normal men carried out while this manuscript was in press yielded a value of 489 ohms-cm for ρ with a standard deviation of 54 7 ohms-cm Use of this revised value of ρ would cause the values of transfer impedance in TABLE 7 to be changed slightly

EXPLORATORY LEAD SYSTEMS AND "ZERO POTENTIALS"*

By Robert H Bayley
University of Oklahoma School of Medicine Oklahoma City Okla

Whenever a vector quantity can be represented by the negative gradient of a scalar quantity the scalar is said to be the potential of the vector In electrical science attention is focused upon the vector $\vec{J}$† known as the current density and upon its potential I In a conservative force field the line integral of $\vec{J}$ along any path from an arbitrary point 1 to an arbitrary point 2 is equal to the difference of the potential at the initial and at the end points of the path (FIGURE 1) In this sense there can be only potential differences[1] The location of points 1 and 2 in the conservative force field is arbitrary It is customary however for authors of texts on electrical theory to choose point 1 as a variable point and to choose point 2 as any point in the force field where the value of the current density $\vec{J}$ is negligible in comparison with its value or with its variations at point 1 The work done (potential) in bringing a positive test particle from outside of the force field to a point 2 in the force field where the current density is negligible, itself amounts to little and the potential vanishes or is zero at the point 2

In the force field of a current dipole that is imbedded in a volume conductor it must always be possible to pass between the poles a surface that divides the conductor into two parts and renders the current density negligible at every point in this surface FIGURE 1 depicts Wilson's choice in this matter We observe that the path from the variable point 1 travels to the zero potential surface and that this surface rotates with the axis of the cardiac dipole and is therefore not a fixed point in the conductor The path continues along this surface to the point 2 at the dipole mid point The potential at the mid point is defined as the average value of the potential of the poles By definition the dipole is composed of a single source and sink of equal magnitude and opposite sign The average value of the pole potential is therefore zero‡ The Wilson central terminal is no more than a method of approximating the potential of the mid point of the equivalent cardiac dipole[2,4] Similarly in electrocardiography a unipolar lead may be defined as the potential difference between a variable point and a fixed point in which the potential variations of the fixed point are equivalent to those of a region of the force field wherein current density is negligible in comparison to its variations at the variable point Unipolar direct leads wherein the variable point is upon the heart's surface or within its substance and where the fixed point is upon a limb certainly meet these requirements to a satisfactory degree and the Wilson central terminal is

* The investigations reported in this paper were supported in part by grants from the National Heart Institute of the National Institutes of Health Public Health Service Department of Health Education and Welfare Bethesda Md and the Oklahoma State Heart Association Oklahoma City Okla

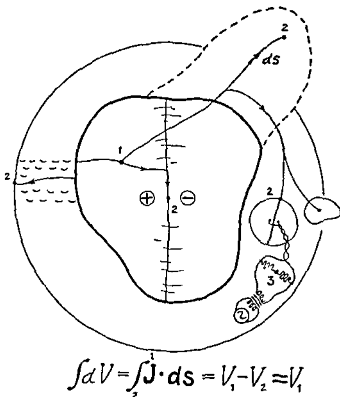
† The symbol over any character designates vector quantity

‡ The potential of the mid point differs from that at infinity by an arbitrary constant nothing is gained and symmetry is lost by choosing an uncustomary value other than zero for this constant

an ideal fixed point for these leads From a clinical point of view the Wilson central terminal is likewise a highly satisfactory reference point with which to explore the variable standard precordial points[5]

An electrode of high conductivity assumes the average value of the potential of the region upon which it rests FIGURE 1 depicts my choice of a path from the variable point to the spherical copper screen 2′ which contains the subject and a homogeneous conducting medium More recently Frank and Kay have chosen a path from the variable point 1 to the extremity of the fixed zero potential plane 2 of the idealized model and after fixing a point 3 of equivalent potential upon the generating circuit of the current dipole have transferred this circuit with the reference potential at 3 over to a volume conductor of irregular boundary for the purpose of mapping the potential distribution[6,7]

We have not been able experimentally to confirm or refute the potential



$$\int dV = \int_2^1 \mathbf{J} \cdot d\mathbf{s} = V_1 - V_2 \approx V_1$$

FIGURE 1 Equivalent cardiac dipole imbedded in a homogeneous volume conductor All path shown for the line integral of the *current density* have the initial variable point 1 The end points of the paths are different Point 2 is fixed at a region of negligible current density presumably at some great distance from the dipole Point 2 is at the dipole midpoint Point 2 is on a spherical *integrating electrode* Point 2 is on the zero-potential plane of the idealized model

measurements of a torso model using a bridge of this general type[6] Theoretical computations for the field of a mathematical dipole indicate however that the average value of the potential of the lead vector components *C* and *C* for 16 points (or electrodes *A I* [7]) on the circumference of the torso model chest at the heart level (by approximate formula) or upon the boundary of the appropriate oblate spheroidal section (by exact formula) bears a sign similar to that pole of the unit dipole which is nearest to the chest circumference[8] (see APPENDIX) By contrast the average value of the potential of the lead components (*C* and *C*) for all dipole positions measured by Frank and Kay[6] with this bridge shows a sign similar to that of the pole of the dipole that is furthest from the chest boundary Frank s tables[7] appear therefore to contain a substantial error in potential measurement that increases in magnitude with that of the absolute value of the potential measured This results in a value short of the true value which fails to show either at zero check in the reference tank or with a reversal of the dipole axis *

If the bridge detector branch admits virtually any current to the zero potential reference (ground) through the capacity of the lead cables or through the detector the error in question is explained Experiments in my laboratory show that if the detector input is through a cathode follower that operates with an input impedance of 10 to 20 thousand megohms and if the current from the dipole field to ground through the detector cable capacitance is virtually eliminated by use of an inner shield (between the cable conductor and the outer ground shield) connected to the cathode of the cathode follower this Kelvin type bridge should measure potential satisfactorily Accuracy is then limited primarily by the mechanical features of the symmetrical reference model or by unstable contact impedance (polarization) at the dipole electrodes The driven shield and the cathode follower prevent further unequalization after zero set of the two voltages from the transformer secondary to the zero reference potential at ground when the bridge is used as a potential measuring device

The circuit may be improved further by connecting the transformer secondary terminals to the two grids of a push pull cathode follower stage that contains two auxiliary series R C bridge arms between the balanced output of the followers The node at the junction of the auxiliary bridge arms is connected in turn to a monitor detector through a third cathode follower The monitor-detector compares the potential of the node to that of ground The auxiliary arms are balanced with the main bridge arms and potential measurements may now be made with confidence on the main detector branch as long as the monitor detector shows no signal Here the only parameter that escapes a signal on the monitor is the slow swing of the dipole contact impedances[9]

Previous immersion experiments by other investigators had the objective of defining the magnitude and sign of the maximum potential on the Wilson

* This is one of several serious objections that are apparent from examination of the potential distributions ascribed by these tables to the torso model A second objection involves the locations of the zero-potential contour lines and a third involves a signal of error on the monitor detector of the auxiliary bridge arms upon rotation of the eccentric-dipole axis due to current in the detector branch

central terminal Their various results determined this error to be of the order of several tenths of a millivolt of negative potential[4, 10-12] The objective of my immersion studies was to determine if weighting a central terminal by unequal resistances might adjust its potential to that of the spherical screen The potential of the screen can be put in the form

$$V_0 = \frac{1}{4\pi R^2} \iint V_P \, ds \tag{1}$$

wherein R is the radius of the screen surface S and V_P is the potential at any point of the region of S produced by a complex of dipoles located within the contained medium If the medium within the sphere is effectively homogeneous the integral in EQUATION 1 vanishes and V_0 is zero If the medium is not effectively homogeneous the residue of the integral may be made negligible by taking R sufficiently large in the construction of the spherical screen

In each immersion experiment an attempt was made to satisfy the relation

$$(V_{TW} - V_0) = 0 \tag{2}$$

that is a detector connected to the central terminal of the potential V_{TW} and to the screen shows no potential difference When EQUATION 2 is satisfied by a given experiment it may be argued that $V_{TW} = V_0 = 0$ for it is not possible for V_0 and V_{TW} to vary in the same way as the field axis varies its direction and magnitude

One objection that can be made to the immersion experiment is that the potentials at the body surface electrodes decrease proportionally in magnitude This objection was overcome by using a differential pre amplifier for the Sanborn two beam photographic detector In our experiments the two units were operated with an over all sensitivity of 7 cm deflection per millivolt Another more serious objection to the immersion experiment is that immersion alters the current distributions within the body of the subject under study by imposing a different boundary condition upon the force field In terms of the normal derivative of the potential V_1 of the subject and the normal derivative of the potential V_2 of the exterior medium the boundary condition is described by the relation[13]

$$\left(\frac{\partial V_1}{\partial \eta} = \frac{K_1}{K_2}\frac{\partial V_2}{\partial \eta}\right)_{-1-} \tag{3}$$

The ratio K_1/K_2 is the specific resistance of the subject to that of the immersion medium If the subject is in air $K_2 >>> K_1$ the right hand side of EQUATION 3 vanishes indicating that no currents produced by the heartbeat extend beyond the body surface When the immersion fluid is Oklahoma City tap water the ratio is about one third at the temperature utilized For distilled water at 37 C the ratio is 1/625 and for a medium of specific resistance equal to that of the subject the ratio is unity

The extreme values of the ratio are zero and unity and the effect of tap water lies somewhere between these values The possibility of using distilled water

was rejected primarily because a single t k would have cost upwards of one thousand dollars

We may examine theoretically the t he zero-potential surface contour on the sphere under the ext er ero and unity for the ratio $K_1/K_{\sim}$ when a dipole with its axis p r e 1 rection of eccentricity is located at a distance equal to one h f the pherical conductor (FIGURE 2) The distance separat 1 ential surface contours is 0 0S of the radius along the axis of e This would correspond to a distance of about 1 cm for the adu Moreover the separation of the zero potential contour vanish whenever the zero-potential surface divides the condu nearly symmetrical parts. Consequently the equipotential cont $\hat{E}$ component of the heart's field are judged to be more sensitive on effect than those of the $\hat{E}$ and $\hat{E}_y$ components and the effe our changes upon the limb electrodes with immersion is that of e dipole eccentricity along the negative Z axis This error 1 t 1 e n of agreement with torso-model measurements The res tat e erminal branch that is connected to the back electrode might the ei neasured by sphere immersion at too large a positive or too small a re ve value Body symmetry with respect to dipole eccentricity indicates n t immersion effect upon the re-

FIGURE 2 The two zero potential surface contours produced by a current dipole eccentric along the negative axis f Z f r a distance f R 2 with the dipole axis parallel to the direction of eccentricity The contour for air is more centrally located by a distance of 0 0S R on the axis f eccentricity As the dipole axis rotates perpendicular to the axis of eccentricity the contour for air coincides with the fixed contour for a similar extensive immersion medium

sistances to the left arm and left leg electrodes should be less than that f the resistance to the back electrode the tendency if any is to measure t resistance for the left leg electrode small with respect to those for the ar electrodes and to measure the resistance for the left arm electrode large wi respect to that for the right arm electrode

The results of the immersion experiments are summarized in FIGURE 3 F the subjects upon whom a null balance was obtained in satisfying EQUATION it may safely be concluded that the orientation of the equivalent cardiac dipo is at the front face or within the voltage tetrahedron based upon the limb a back electrodes[14-17] For subjects upon whom the null balance was not o tained there remains the possibility that the orientation of the equivale cardiac dipole may lie exterior to the Burger voltage tetrahedron The first these conclusions is based upon the null balance reached in two thirds of t group of normal young adult subjects and appears to be in rather serious d agreement with the conclusions reached by Frank[7, 21] Frank and Kay[22] a McFee and Johnston[18-20] which are based upon an entirely different approa to the problem of solving heart dipole orientation The sphere immersi studies incidentally show a common orientation for the heart vector of ventric lar accession and ventricular regression and minimize the importance of var ble eccentricity of the equivalent cardiac dipole except as associated with r piration

The chief advantage of the method is that the desired information on ori tation of the equivalent dipole is embodied in one null detection operati Inasmuch as the potential at any point on the surface of the homogeneo volume conductor of arbitrary shape due to an imbedded dipole is by fir order approximation twice the value that would obtain at the same point the extent of the conductor were infinite the sphere immersion method w $K_1/K_2 = 1/3$ may be considered as yielding a good first-order result

It is logical that the substitution of distilled water for tap water shou improve the accuracy of the results well beyond a first order approximati and the cost would be reasonable for use of the sphere immersion method w certain laboratory animals and for the force field produced by the isolated he embedded in a homogeneous fluid medium

The Grid Lead Central Terminal

It is my purpose to describe a central terminal the construction of wh embodies certain of the theoretical and experimental ideas of McFee a Johnston[18-20] of Frank[7, 21] and of Frank and Kay[22] and of the sphere immers experiments[15] From the first of these sources we have adopted a grid ty electrode in which some 250 studs are arranged symmetrically on an elas belt (FIGURE 4) Each stud is connected to the grid terminal of potent V_{T_2} through equal resistances of 1 million ohms The contact face of ea stud is circular and the contact area 1 0 3 cm The skin is rubbed bris with electrode paste and then is wiped dry No paste is applied directly to studs An even waffle iron skin pattern is obtained by the elasticity of belt and by firmly lacing 2 sponge rubber pads exterior to the belt one at

was rejected primarily because a single tankful would have cost upwards of one thousand dollars

We may examine theoretically the positions of the zero potential surface contour on the sphere under the extreme values of zero and unity for the ratio K_1/K_2 when a dipole with its axis parallel to the direction of eccentricity is located at a distance equal to one half of the radius of the spherical conductor (FIGURE 2) The distance separating the zero potential surface contours is 0 08 of the radius along the axis of eccentricity[14] This would correspond to a distance of about 1 cm for the adult human subject Moreover the separation of the zero potential contour lines tends to vanish whenever the zero potential surface divides the conductor into two nearly symmetrical parts Consequently the equipotential contour lines of the $\hat{E}$ component of the heart s field are judged to be more sensitive to the immersion effect than those of the $\hat{E}$ and $\hat{E}_y$ components and the effect of these contour changes upon the limb electrodes with immersion is that of increasing the dipole eccentricity along the negative Z axis This error is in the direction of agreement with torso model measurements[7] The resistance h in the terminal branch that is connected to the back electrode might therefore be measured by sphere immersion at too large a positive or too small a negative value Body symmetry with respect to dipole eccentricity indicates that the immersion effect upon the re

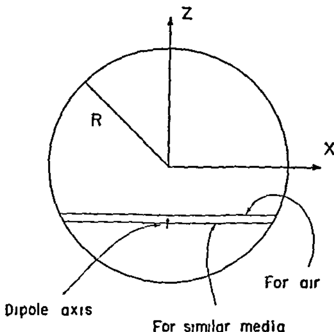


FIGURE 2 The two zero-potential surface contours produced by a current dipole eccentric along the negative axis of Z for a distance of $R/2$ with the dipole axis parallel to the direction of eccentricity The contour for air is more centrally located by a distance of 0 08 R on the axis of eccentricity As the dipole axis rotates perpendicular to the axis of eccentricity the contour for air coincides with the fixed contour for a similar extensive im

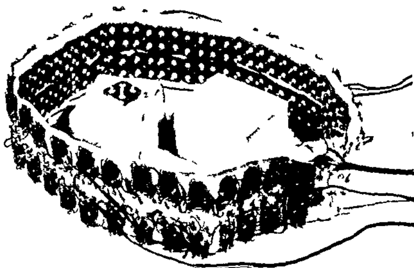


FIGURE 4 A grid lead central terminal composed of symmetrically arranged studs in an elastic belt each connected to a common node of potential V_{T0} through a resistance of one million ohms Each gold band ohmite carbon resistor is soldered directly to a stud The summing conductor loops along the binding posts (1 per 4 studs) for a soldered contact and then doubles back to avoid an induction ring Each unit of 4 studs 4 resistors and 1 binding post is fixed in a low loss dielectric board The studs are at the corners of a 1 5 cm square with central binding post

mid line anteriorly and one posteriorly The skin resistance through a single stud is about 100K ohms and the series parallel resistances through adjacent studs with the belt in place are uniform within a 10 per cent variation In accordance with the suggestions of Frank and his associates the long axis of the belt is applied carefully on the circumference of the chest at the level of the sternal end of the 5th intercostal space and is then leveled with a plumb bob suspended by a string In this way the E component of the heart s field is essentially eliminated[7]

Adopted from the sphere immersion principle is the 2 dimensional version of EQUATION 1 If the body medium is effectively homogeneous and if the studs are on a circular boundary the integral vanishes due to the potential of any complex of dipoles contained in the plane of the circular circumference The 4 rows of studs give 4 such circumferences that cover the vertical dimensions of the field source The actual noncircular configuration of the boundary should introduce only small off zero values for the potential V_{T0} due to intra cardiac dipoles of limited or normal eccentricity

As an illustration of the method for estimating the error on V_{TG} use is made of the components of the lead vector table prepared from the data of Frank[7] (FIGURE 5) as explained earlier in this article Nevertheless it appears likely that the off zero value of V_{TG} is less than the potential of the Wilson central terminal

Several uses for the grid lead central terminal suggest themselves The potential of the Wilson terminal may be evaluated by leads of the form

$$(V_T - V_{TG}) \tag{4}$$

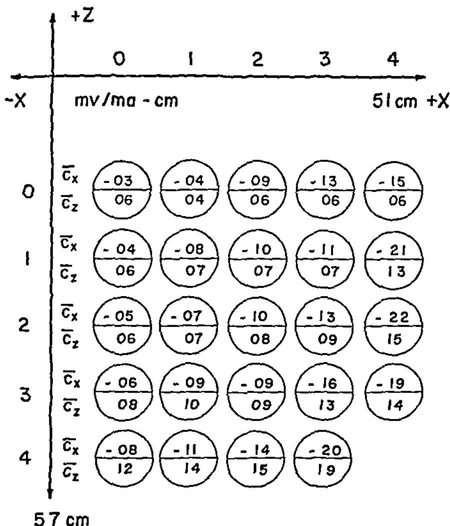


FIGURE 5 Diagram of the average absolute values of the components of the 16 unipolar lead vectors for electrodes A through P[7] For any dipole position shown these components require multiplication by the corresponding dipole component in ma cm and the sum of the products thus determined gives the potential on the grid lead terminal for that dipole orientation For dipole 13 $P \approx 0$ when P is 0 7[7] and the maximum error of V_{TG} is 0 7 (0 1) = 0 07 mv For dipoles 10 12 and 23 V_{TG} is 'Zero if maximum $P = P$

The resistances in the Wilson terminal may be adjusted for minimal values of the potential difference

$$(V_{rw} - V_{ro}) \qquad (5)$$

and the residual potential difference may be ascribed to the off zero value of V_r as produced primarily by the E component of the heart's field. Sphere immersion experiments indicate that this error may be negligible (FIGURE 3) in a majority of young adult subjects. Measurements on the torso model by Frank and Kay[22] exclude the possibility of a zero potential in the weighted or unweighted three branch Wilson terminal. Consequently, leads of the kind indicated by EQUATION 5 should prove of considerable interest at this time.

A third type of experiment involves recording the limb and back potentials at three or four times the normal sensitivity, using the grid lead central terminal as a reference. Measurement of these potentials with respect to a common time base such as lead I will then permit a calculation of the resistance ratios that are required to bring a four branch central terminal toward a value of zero, depending, of course, on the accuracy of the grid lead terminal. The equation required for this purpose is of the form[15]

$$\frac{h}{r}\alpha_{123} + \frac{h}{l}\beta_{123} + \frac{h}{f}\gamma_{123} = -\delta_{123} \qquad (6)$$

wherein the resistances r, l, f and h are connected to the limb and back electrodes R, L, F and B respectively. The values of α, β, γ, and δ correspond

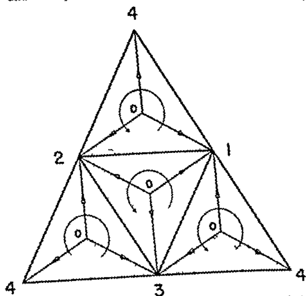


FIGURE 6. Voltage tetrahedron 1234 based on the electrode system 1, 2, 3 and 4 is unfolded to show the subtetrahedra 0234, 0134, 0124 and 0123 whose volumes vary inversely with the resistances r, l, f and h, respectively. In each instance the order of the subscripts for the unipolar lead vectors circulates counterclockwise for the observer stationed at 0 in the interior to the tetrahedron 1234.

to the potentials V_R, V_L, V_F and V_B at the three instants of time indicated by the subscript for three noncoplanar directions of the field axis. The equivalent equation using Frank's vector notation[21] is

$$\frac{h}{r}[\hat{C}_1 \hat{P}_{1\,2\,3}] + \frac{h}{l}[C_2 \hat{P}_{1\,2\,3}] + \frac{h}{f}[C_3 \hat{P}_{1\,2\,3}] = -[\hat{C}_4 \hat{P}_{1\,2\,3}] \qquad (7)$$

wherein $\hat{C}_1$, C_2, $\hat{C}_3$ and C_4 are the constant unipolar lead vectors for the arbitrary four electrode system and $\hat{P}_{1\,2\,3}$ is the variable heart vector at three arbitrary instants of time for three noncoplanar directions. Solving EQUATIONS 6 and 7 gives

$$\left.\begin{aligned}
\frac{h}{r} &= \frac{[C_3\hat{C}_2\hat{C}_4]}{[C_1\hat{C}\,\hat{C}_3]} = \frac{1}{\Delta}\begin{vmatrix} \delta_1\beta_1\gamma_1 \\ \delta\,\beta\,\gamma \\ \delta_3\beta_3\gamma_3 \end{vmatrix} \\
\frac{h}{l} &= \frac{[C_1\hat{C}_3\hat{C}_4]}{[C_1\hat{C}_2\hat{C}_3]} = \frac{1}{\Delta}\begin{vmatrix} \alpha_1\delta_1\gamma_1 \\ \alpha\,\delta\,\gamma \\ \alpha_3\delta_3\gamma_3 \end{vmatrix} \\
\frac{h}{f} &= \frac{[C\,\hat{C}_1 C_4]}{[C_1 C\,\hat{C}_3]} = \frac{1}{\Delta}\begin{vmatrix} \alpha_1\beta_1\delta_1 \\ \alpha\,\beta\,\delta \\ \alpha_3\beta_3\delta_3 \end{vmatrix}
\end{aligned}\right\} \qquad (8)$$

$$\Delta = \begin{vmatrix} \alpha_1\beta_1\gamma_1 \\ \alpha\,\beta_2\gamma_2 \\ \alpha_3\beta_3\gamma_3 \end{vmatrix}$$

	A	B	C	Torso
0123	-25	-12	-3741	-3153
0324	430	156	1355	1350
0134	734	268	5823	4756
0214	520	16.8	1602	4793
Index	16	095	15	132

FIGURE 7. Top frame shows the voltage tetrahedral volumes for subjects A, B, C and for similar data on the torso model.[21] The index is the ratio of transverse/anteroposterior thoracic diameters at the heart-dipole level.

A	(r=17 l=12 f=-0 06 h) (r=5 l=12 f), $(V_{TW}-V_{TG})$=0 06 MV (P-P)
B	(r=17 l=10 f=-0 07 h) (r=5 l=16 f), $(V_{TW}-V_{TG})$=0 07 MV (P-P)
C	(r=43 l=12 f=-28 h) (r=10 l=10 f), $(V_{TW}-V_{TG})$=0 28 MV (P-P)
Torso model	(r=35 l=35 f=-23 h) (r=11 l=11 f)

FIGURE 8 Resistance ratios by EQUATION 8 and by the null balance with the Wilson terminal resistance on the potential difference $(V_{TW} - V_{TG})$ The residual unbalance is given in millivolts and is ascribed primarily to the F component of the heart's field When volume 0123 is negative the residual unbalance is of the − + form with ordinary behavior of the heart vector

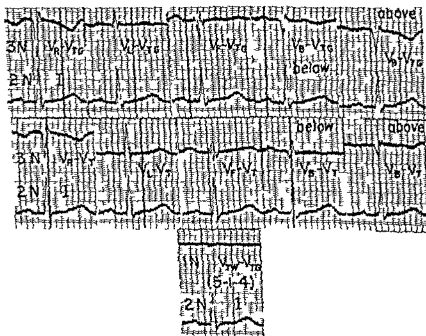


FIGURE 9 Electrocardiogram of subject A from which the potential measurements in FIGURE 12 were taken The values for B are the average of the potentials recorded from below and above the grid lead belt 1 cm to the left of the spine The arbitrary choice of time on lead I is important and should avoid maximum and small values in the unipolar leads thus, errors on small potentials are not multiplied manyfold during computation by EQUATION 8 The measurements are charted in FIGURES 8 and 12

FIGURE 10 Electrocardiogram of subject *B* as in FIGURE 9

FIGURE 11 Electrocardiogram of subject *C* as in FIGURE 9

Each quantity in square brackets is a scalar triple product of three vectors and each such quantity is equivalent to six times the volume of a tetrahedron wherein the indicated vectors join the vertices from a common origin O The signs have been handled in the customary way[23] so that an observer stationed at the origin views the opposite face of the tetrahedron and the subscript from left to right circulates the positive area counterclockwise (FIGURE 6) The four subtetrahedra 0324 0134 0214 and 0123 form the large Burger voltage tetrahedron 1234 based on the four electrode system When the origin O of the C and $\hat{P}$ vectors is exterior to a given face of 1234 the order of the subscript circulates clockwise (FIGURE 6) In certain respects the solution (EQUATION 8) appears more general than that recently offered by Marchand and his associates[4] which is derived from three particular directions of the unit heart vector

		A	B	C
$(V_R)_1$	α_1	-8	1	0
$(V_R)_2$	α_2	-115	-10	-13
$(V_R)_3$	α_3	1	-4	3
$(V_L)_1$	β_1	17	-05	-17
$(V_L)_2$	β_2	27	-2	-17
$(V_L)_3$	β_3	-05	-1	-05
$(V_F)_1$	γ_1	-36	-03	-17
$(V_F)_2$	γ_2	-35	16	15
$(V_F)_3$	γ_3	33	7	13
$(V_B)_1$	$\frac{\delta_1+\delta_1}{2}$	-85	-12	-33
$(V_B)_2$	$\frac{\delta_2+\delta_2}{2}$	-25	45	-4
$(V_B)_3$	$\frac{\delta_3+\delta_3}{2}$	23	3	-65

FIGURE 12 Measured values of simultaneous potentials from the grid lead set of QRS deflections in FIGURES 9 10 and 11

The results of a study of subjects A B and C are shown in FIGURE 7, together with the corresponding data computed from the torso model measurements of Frank for comparison The tetrahedral volumes are quite similar in subjects A and B and the small volumes of 0123 indicate that the heart dipole is at the voltage 123 triangle of the tetrahedron 1234 The volumes for subject C compare favorably with those of the torso model The major difference here is in the volume 0214 which varies inversely with the resistance to the left leg electrode The index is determined by dividing the transverse axis of the chest by the anteroposterior axis at the heart level FIGURE 8 shows the solutions for the resistance ratios computed from the potential measurements and the same ratios determined by adjusting the three or four branch terminal for a null of the potential difference ($V_{TW} - V_{TG}$)

The electrocardiograms for subjects A B and C appear in FIGURES 9 10

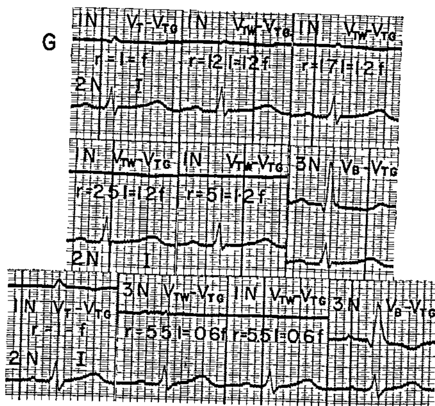


FIGURE 13 In reading order the curves $V_{TW} - V_{TG}$ display the stepwise null balance ocedure conducted for subject G The result $r = 2\ 5l = 1\ 2f$ locates the equivalent cardiac pole in the Burger voltage triangle 123 (FIGURE 6) to an accuracy limited by that of the d lead central terminal Lead $V_B - V_{TG}$ indicates that a reasonably large F component tually exists The B electrode is just to the left of the spine below the grid belt Subject with $V_{TW} - V_{TG}$ is recorded three times the normal value The result $r = 5\ 5l = 0\ 6f$ cates the equivalent cardiac dipole within the Burger voltage triangle

and 11 respectively The data obtained by the attempted null balance must be regarded as considerably more accurate than those determined by measurement of potentials for EQUATION 8 These measurements could be improved however by using a four channel photographic recorder with a delicate time line indicator FIGURE 12 shows the measured values of simultaneous potentials from the grid lead set of QRS deflections in FIGURES 9 10 and 11 A null balance of the kind shown in FIGURE 13 gives an indication of the sensitivity response to adjustments of 10K ohm steps and ultimately satisfies the equation $(V_{TW} - V_{TG}) = 0$ for subject G

FIGURE 14 summarizes the results of balance operations on a group of normal adult male subjects The average values of the ratios are interesting in that the coefficients for the left leg are close to those of the sphere immersion measurements while those for the left arm are not With the grid lead terminal reference the coefficient for the h resistance is probably negative in most of the subjects studied but like the sphere immersion measurements orienta

Subject	$(V_T - V_{TG})$ millivolts P P	$(V_{TW} - V_{TG})$ millivolts P-P	Ratios	Index Trans/A P
A	0 45	0 06	r=5 l=1 2 f	1 6
B	0 20	0 07	r=5 l=1 6 f	0 95
C	0 50	0 28	r=10 l=f	1 5
D	0 33	0 12	r=1 6 l=1 0 f	1 43
E	0 13	0 10	r=1 6 l=f	1 29
F	0 30	0 02	r=5 5 l=0 6 f	1 25
G	0 13	0 03	r=2 5 l=1 2 f	1 32
H	0 50	0 40	r=5 l=f	1 32
I	0 15	0 10	r=2 5 l=1 2 f	1 46
J	0 40	0 27	r=4 5 l=1 1 f	1 47
K	0 30	0 20	r=2 3 l=1 4 f	1 09
L	0 40	0 27	r=10 l=2 5 f	1 52
Avg	0 32	0 16	r=4 6 l=2 f	—

FIGURE 14 Summary of the attempted null balance operations on the potential difference between the weighted central terminal potential V_{TW} and the potential V_{TG} of the grid lead central terminal in a group of normal adult males

tion of the equivalent cardiac dipole appears to be near the plane of the Burger voltage triangle [5, 25b]

Discussion and Conclusions

The grid lead central terminal is based on reasonably sound theoretical and experimental data [7, 15, 18, ??] its use as a reference potential for evaluating the orientation of the equivalent cardiac dipole is described Its construction can undoubtedly be improved Several varieties of weighting of the grid lead terminal may be necessary to cover unusual dipole orientations In a given subject the equivalent cardiac dipole orientation is computed in terms of the resistances in the branches of a central terminal for a three or four electrode system When the preliminary results are compared with those of the sphere immersion experiments the latter being regarded as a good first order approximation the direction of the theoretical error of sphere immersion measurements is supported by the grid lead terminal measurements

Orientation of the equivalent cardiac dipole from subject to subject as determined by the grid lead central terminal appears to include those orientations determined by the sphere immersion studies as well as those determined from a homogeneous torso model The coefficient in the left arm branch of the Wilson terminal is distinctly higher by grid lead central terminal measurement than by sphere immersion measurement The coefficient for the resistance in the left leg branch of the Wilson terminal is somewhat lower by grid lead central terminal measurement than by sphere immersion measurement A fourth branch to the Wilson terminal which is connected to a back electrode is determined by both methods to be of little or no value in bringing the potential of the Wilson terminal toward that of the grid lead central terminal When the reference potential is that of the immersion sphere and when it is that of the grid lead central terminal the apparent orientation of the equivalent cardiac dipole is frequently at the voltage plane of the Burger triangle

The potential of the Wilson central terminal with reference to the grid lead central terminal varies considerably from subject to subject and averages 0 32 mv in a small group of normal male adult subjects The potential difference with the weighted three branch Wilson terminal is about half of this value and indicates a small error on the Wilson terminal that may be ascribed to the z component of the heart s field

The reference potential on the dipole generating circuit is apparently unsound as Frank and Kay have used it [6] and a bridge circuit that may be used to measure toroso model potentials accurately is described

Appendix N M Space Harmonics of the Oblate Spheroid

By Paul M Berry

Heart Station University Hospital Oklahoma City Okla

The original problem proposed by Bayley can be stated as follows a known doublet direct current source is located inside a homogeneous and finitely conducting body The conductor is imbedded in a perfect dielectric medium

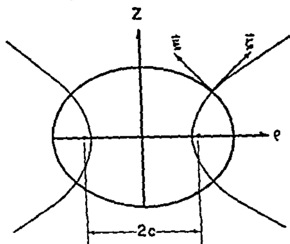


FIGURE 15 The oblate spheroidal coordinate system Vector ζ is the unit vector normal to the ellipse and ξ is the unit vector normal to the hyperboloid Distance 2c is the distance from one focal point to the other

The position and orientation of the doublet is arbitrary It is desired to determine the potential distribution on the surface of the conducting body

Here the conducting body will be taken as an oblate spheroid The potential distribution will satisfy Laplace s equation with the boundary condition of zero normal gradient Thus the problem is to solve

$$\nabla^2\phi = 0 \tag{1}$$

with

$$\frac{\partial\phi}{\partial\eta} = 0 \tag{2}$$

L J Chu [6] obtained a solution to the problem that will be outlined here Consider an oblate spheroidal coordinate system as shown in FIGURE 15 The equation of the spheroids is

$$\frac{x^2}{\zeta^2} + \frac{\rho^2}{\zeta^2 + 1} = c^2 \qquad \zeta \geq 0 \tag{3}$$

and that of the hyperboloids is

$$\frac{x^2}{-\xi} + \frac{\rho^2}{1 - \xi^2} = c^2 \qquad -1 < \xi < 1 \tag{4}$$

where c denotes one half of the focal distance Writing Laplace s equation in general orthogonal coordinates one has

$$\nabla^2\phi = h_1 h_2 h_3 \left\{ \frac{\partial}{\partial\rho_1}\left(\frac{h_1}{h_2 h_3}\frac{\partial\phi}{\partial\rho_1}\right) + \frac{\partial}{\partial\rho_2}\left(\frac{h_2}{h_3 h_1}\frac{\partial\phi}{\partial\rho_2}\right) + \frac{\partial}{\partial\rho_3}\left(\frac{h_3}{h_1 h_2}\frac{\partial\phi}{\partial\rho_3}\right)\right\} = 0 \tag{5}$$

Writing the coordinates in the order, ξ ζ ϕ the metrical coefficients are

$$h_1 = \frac{ds_1}{d\xi} = c\left(\frac{\xi^2 + \zeta^2}{1 - \xi^2}\right)^{\frac{1}{2}} \tag{6}$$

$$h_2 = \frac{ds_2}{d\zeta} = c\left(\frac{\xi^2 + \zeta^2}{1 + \zeta}\right)^{\frac{1}{2}} \tag{7}$$

$$h_3 = \frac{ds_3}{d\phi} = c[(1 + \zeta^2)(1 - \xi^2)]^{\frac{1}{2}} \tag{8}$$

As was shown by Smythe[7] the general solution of Laplace s equation in this system can be written as

$$\phi = \sum_{=0}^{\infty} \sum_{m=0} R_{m}\Theta_{m}\Phi_m \tag{9}$$

where

$$R_m = AP^m(j\zeta) + BQ^m(j\zeta) \qquad j = \sqrt{-1} \tag{10}$$

$$\Theta_m = CP^m(\xi) + DQ^m(\xi) \tag{11}$$

$$\Phi_m = E\cos m\phi + F\sin m\phi \tag{12}$$

P^m and Q^m are the associated Legendre functions of the first and second kind The potential at a point $P(\xi\ \zeta\ \phi)$ due to a unit charge at a point $Q(\xi_0\ \zeta_0\ \phi_0)$ can be expressed as follows[7]

$$\phi_q = \begin{cases} \frac{1}{c}\sum_{=0}^{\infty}\sum_{m=0} j(2 - \delta_m^0)(-1)^m(2n + 1)\left[\frac{(n - m)!}{(n + m)!}\right] & (13) \\ \quad P^m(j\zeta)P^m(\xi)Q^m(j\zeta_0)P^m(\xi_0)\cos m(\phi - \phi_0) \quad \zeta < \zeta_0 & \\ \frac{1}{c}\sum_{=0}^{\infty}\sum_{m=0} j(2 - \delta_m^0)(-1)^m(2n + 1)\left[\frac{(n - m)!}{(n + m)!}\right] & (14) \\ \quad Q^m(j\zeta)P^m(\xi)P^m(j\zeta_0)P^m(\xi_0)\cos m(\phi - \phi_0) \quad \zeta > \zeta_0 & \end{cases}$$

As[8]

$$\phi_p = p\ \nabla_0\phi_q \qquad p = \text{dipole moment} \tag{15}$$

the potential at P due to a doublet at Q can be written as

$$\phi_p = \begin{cases} \frac{1}{c}\sum_{=0}^{\infty}\sum_{m=0}^{n} j(2 - \delta_m^0)(-1)^m(2n + 1)\left[\frac{(n - m)!}{(n + m)!}\right] & (16) \\ \quad P^m(j\zeta)P^m(\xi)p\ \nabla_0[Q^m(j\zeta_0)P^m(\xi_0)\cos m(\phi - \phi_0) \quad \zeta < \zeta_0 & \\ \frac{1}{c}\sum_{=0}^{\infty}\sum_{m=0} j(2 - \delta_m^0)(-1)^m(2n + 1)\left[\frac{(n - m)!}{(n + m)!}\right] & (17) \\ \quad Q^m(j\zeta)P^m(\xi)\hat{p}\ \nabla_0[P_n^m(j\zeta_0)P^m(\xi_0)\cos m(\phi - \phi_0) \quad \zeta < \zeta_0 & \end{cases}$$

EQUATION 17 is chosen as the potential of the primary field In addition to this there is a secondary field caused by the discontinuity of the finite conducting spheroid Except for an appropriate coefficient the secondary field must be of the same form as EQUATION 16 The coefficient is determined from the boundary condition EQUATION 2 Explicitly the secondary field must be of the form

$$\phi_p = \frac{1}{c}\sum_{n=0}^{\infty}\sum_{m=0}^{n} j(2-\delta_m^0)(-1)^m(2n+1)\left[\frac{(n-m)!}{(n+m)!}\right]^2 \left[-\frac{Q_n^{m\prime}(j\zeta_1)}{P_n^{m\prime}(j\zeta_1)}P_n^m(j\zeta)\right]P_n^m(\xi)p\cdot\nabla_0[P_n^m(j\zeta_0)P_n^m(\xi_0)\cos m(\phi-\phi_0)] \tag{18}$$

where ζ_1 denotes the value of ζ defined at the surface of the conducting spheroid and the prime denotes the derivative with respect to ζ The resultant potential is then given by

$$\phi_{\zeta=\zeta_1} = \frac{1}{c}\sum_{n=0}^{\infty}\sum_{m=0}^{n} j(2-\delta_m^0)(-1)^m(2n+1)\left[\frac{(n-m)!}{(n+m)!}\right]^2 \left[Q_n^m(j\zeta_1)-\frac{Q_n^{m\prime}(j\zeta_1)}{P_n^{m\prime}(j\zeta_1)}P_n^m(j\zeta_1)\right]P_n^m(\xi)p\cdot\nabla_0[P_n^m(j\zeta_0)P_n^m(\xi_0)\cos m(\phi-\phi_0)] \tag{19}$$

With the aid of the Wronskian of the associated Legendre functions[7] namely,

$$P_n^m(j\zeta)Q_n^{m\prime}(j\zeta) - Q_n^m(j\zeta)P_n^{m\prime}(j\zeta) = \frac{j(-1)^m}{1+\zeta^2}\frac{(n+m)!}{(n-m)!} \tag{20}$$

the value of $\phi_{\zeta=\zeta_1}$ can be further simplified That gives

$$\phi_{\zeta=\zeta_1} = \frac{1}{c}\sum_{n=0}^{\infty}\sum_{m=0}^{n}(2-\delta_m^0)(2n+1)\frac{(n-m)!}{(n+m)!}\frac{1}{1+\zeta_1^2}\frac{P_n^m(\xi)}{P_n^{m\prime}(j\zeta_1)}p\cdot S_{nm} \tag{21}$$

where

$$S_{nm} = \frac{1}{c}\left(\frac{1-\xi_0^2}{\xi_0^2+\zeta_0^2}\right)^{1/2}P_n^m(j\zeta_0)P_n^{m\prime}(\xi_0)\cos m(\phi-\phi_0)\xi_0 + \frac{1}{c}\left(\frac{1+\zeta_0^2}{\xi_0^2+\zeta_0^2}\right)^{1/2}P_n^{m\prime}(j\zeta_0)P_n^m(\xi_0)\cos m(\phi-\phi_0)\zeta_0 + \frac{1}{c}[(1+\zeta_0^2)(1-\xi_0^2)]^{-1/2}P_n^m(j\zeta_0)P_n^m(\xi_0)m\sin m(\phi-\phi_0)\phi_0 \tag{22}$$

In these equations ξ_0 ζ_0 ϕ_0 are unit vectors along the direction of increasing ξ_0 ζ_0 and ϕ_0 respectively The prime denotes the derivative with respect to ξ_0 or ζ_0

Chu also applied the preceding formulation to prolate spheroids [6] If one arranges the prolate spheroidal coordinates in the order ξ η and ϕ with the metrical coefficients given by

$$h_1 = \frac{ds_1}{d\xi} = c\left(\frac{\eta^2 - \xi^2}{1 - \xi^2}\right)^{\frac{1}{2}} \tag{23}$$

$$h_2 = \frac{ds_2}{d\eta} = c\left(\frac{\eta^2 - \xi^2}{\eta^2 - 1}\right)^{\frac{1}{2}} \tag{24}$$

$$h_3 = \frac{ds_3}{d\phi} = c[(1 - \xi)(\eta^2 - 1)]^{\frac{1}{2}} \tag{25}$$

then the potential at a point $I(\xi\ \eta\ \phi)$ on the surface of a prolate spheroid due to a doublet at $Q(\xi_0\ \ \eta_0\ \ \phi_0)$ can be shown to be given by

$$\phi_{\eta\ \ \xi} = -\frac{1}{c}\sum_{=0}^{\infty}\sum_{m=0}(2 - \delta_m^0)(2n + 1)\frac{(n - m)!}{(n + m)!}\frac{1}{\eta^2 - 1}\frac{P^m(\xi)}{I^m(\eta)}\,p\ \ Tnm \tag{26}$$

where

$$Tnm = \frac{1}{c}\left(\frac{1 - \xi_0^2}{\eta_0 - \xi_0^2}\right)^{\frac{1}{2}} P^m(\eta_0)P^m(\xi_0)\cos m(\phi - \phi_0)\xi_0$$
$$+ \frac{1}{c}\left(\frac{\eta_0^2 - 1}{\eta_0^2 - \xi_0}\right)^{\frac{1}{2}} P^m(\eta_0)P^m(\xi_0)\cos m(\phi - \phi_0)\eta_0 \tag{27}$$
$$+ \frac{1}{c}[(\eta_0^2 - 1)(1 - \xi_0^2)]^{-\frac{1}{2}}P^m(\eta_0)P^m(\xi_0)m\sin m(\phi - \phi_0)\phi_0$$

In these equations ξ_0 η_0 and ϕ_0 are unit vectors along the increasing ξ_0 η_0 and ϕ_0 The primes indicate the differentiation of the function with respect to the argument

Chu also derived an approximate solution that applies to a body of arbitrary shape [6] Mathematically one can express the potential function at any point of observation P as

$$\phi = \phi_p - \int_\Omega \tau\, d\Omega \tag{28}$$

where ϕ_p represents the potential due to the dipole inside the surface τ the surface density of the double layer on the surface of the body because of the dipole and $d\Omega$ the differential solid angle at the point of observation subtended by the element of area of integration

For the problem under consideration the approximate solution of the integral equation is

$$\phi \cong 2\phi_p = 2p\ \nabla_0(1/r) \tag{29}$$

wherein the sum of the positive and negative weighted solid angles is neglected Here r is the distance measured from the dipole to the point of observation on the surface In applying the above approximation to an oblate spheroid the approximation can be improved by replacing the terms that are radically off the corresponding exact solution One then has

$$\phi_{\zeta\ \ \xi} \cong 2\phi_p - \frac{1}{c}\sum_n \sum_m j(2 - \delta_m^0)(-1)^m(2n+1)\left[\frac{(n-m)!}{(n+m)!}\right]^2 \left[Q^m(j\zeta) + \frac{Q^m(j\zeta)}{P^m(j\zeta)} P^m(j\zeta)\right] P^m(\xi)p\ Snm \quad (30)$$

Likewise for the prolate spheroids one has

$$\phi_\eta \cong 2\phi_p - \frac{1}{c}\sum \sum_m (2 - \delta_m^0)(-1)^m(2n+1)\left[\frac{(n-m)!}{(n+m)!}\right] \left[Q^m(\eta) + \frac{Q^m(\eta)}{P^m(\eta)} P^m(\eta)\right] P_n^m(\xi)p\ Tnm \quad (31)$$

The double summations are over values of n and m for which EQUATION 29 is not sufficiently accurate

The potentials at 16 points were computed for 2 dipole positions in an oblate spheroid whose ratio of major axis to minor axis was 1 32 with the minor axis of unit length The 16 points were on the plane formed by the ρ and Z axes and were located such that the central angle determined by any 2 adjacent points was 22 5

In the first case the dipole was located at the oblate spheroidal coordinates (−1, 0 232 and 0) or 0 2 of the distance out along the negative Z axis with a unit moment directed along the positive Z axis such that the negative pole was nearest the boundary EQUATION 21 was used for the calculation In this case it simplified to

$$\phi_{\zeta\ \ \xi} = -\frac{1}{c(1+\zeta^2)} \sum_{n=0}^{\infty} (-1)\ (2n+1)\frac{P'(j\zeta_0)}{P'(j\zeta)} P(\xi) \quad (32)$$

For this spheroid ζ equals 1 16 and c equals 0 862

The upper diagram in FIGURE 16 shows the geometrical configuration and the values of the potential at the points in question The average value of the potential is

$$\frac{\sum\phi}{16} = -0\ 186 \quad (33)$$

Only the first 10 terms of the series in EQUATION 32 were used Values for the functions were taken to 4 decimal places and obtained by linear interpolation from *Tables of Associated Legendre Functions* *

In the second case the dipole was located at the oblate spheroidal coordinates

* Columbia University Press 1945 New York N Y

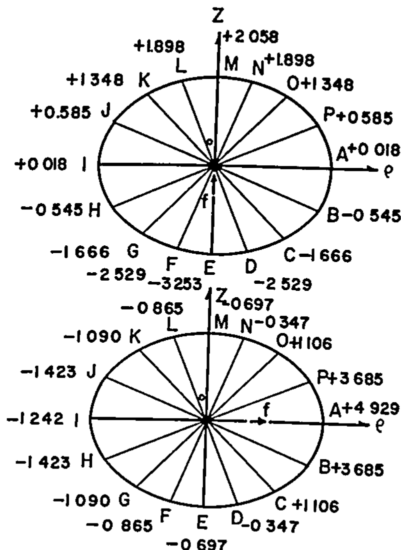


FIGURE 16 The top diagram shows the distribution of the potentials calculated in case 1 when the dipole was at $f = 0\ 2$ of the unit minor hemiaxis along the negative z axis with the positive pole directed toward the origin Potential E is in the middle of the front of the chest and M is in the middle of the back Here the average of the 16 potential is $-0\ 186$ The bottom diagram shows the distribution of the potentials calculated in case 2 when the dipole was at $f = 0\ 46$ of 1 32 the major hemiaxis along the $+\rho$ axis with the positive pole directed toward point A Here the average of the 16 potentials is $+0\ 277$

(0 0 707 and 0) or about 0 46 of the distance out along the $+\rho$ axis with a unit moment directed along the axis such that the positive pole was nearest the boundary EQUATION 30 was used for the calculation In this case it simplified to

$$\phi_{\zeta\ \xi} \cong 2\phi_p - \frac{1}{c^2}\sum \sum_m j(2 - \delta_m^0)(2n + 1)(-1)^m \left[\frac{(n - m)!}{(n + m)!}\right]^2 \tag{34}$$

$$\left[Q^m(j\zeta\ ) + \frac{Q^m(j\zeta_a)}{P^m(j\zeta\ )} P^m(j\zeta_a)\right] P^m(\xi) P^m(0\ j) P_n^m(707)\quad n + m \text{ odd}$$

The values of ζ_a and c are the same It sufficed to take n from 0 to 10 and m from 0 to 3

The lower diagram in FIGURE 16 shows the geometrical configuration and the values of the potential at the points in question The average value of the potential is

$$\frac{\sum\phi}{16} = +0\,277 \tag{35}$$

First to be noted is that in each of these two cases the sign of the average value of the potential was the same as that of the pole of the dipole nearest the boundary It is wise to give a precise definition of the word nearest ' Consider the line of minimum length drawn from the mid point of the dipole to the boundary of the spheroid The pole of the dipole that forms an acute angle with this line will be called the pole nearest the boundary The other pole will be the furthest from the boundary In the case in which the poles of the dipole form a right angle with this line they will be equidistant from the boundary

The preceding work suggests a possible theorem (1) the sign of the average potential over the boundary of an oblate spheroid due to a dipole imbedded in it is the sign of the pole nearest the boundary (2) if the dipole is located at the intersection of the axes of the oblate spheroid the average potential is zero

With case 1 it is well argued that the average potential would be more negative when measured on a true model of the human torso as there are two bulges in the back that make these potentials deviate somewhat from the mathematical model used here These back potentials would be smaller in magnitude while the indentation in the chest at the point of the largest negative potential would make this potential low in magnitude Thus one would expect the average potential to be more negative than in the case computed To make corresponding statements concerning the results found in the second case is more difficult Here the bulges would affect both some positive and some negative potentials while the indentation would increase the magnitude of one of the negative potentials

References

1 HAAS A 1928 Introduction to Theoretical Physics 1 36 Constable & Co London England

2 WILSON F N 1930 The distribution of the potential differences produced by the heart beat within the body and at its surface Am Heart J 5 599

3 WILSON F N F D JOHNSTON A G MACLEOD & P S BARKER 1934 Electroca diograms that represent the potentials variations of a single electrode Am Heart J 9 447

4 WILSON F N F D JOHNSTON F F ROSENBAUM & P S BARKER 1946 On Eint

hoven s triangle the theory of unipolar electrocardiographic leads and the interpretation of the precordial electrocardiogram Am Heart J 32 277
5 BAYLEY R H 1955 The potential variations of the limb back and precordial electrodes with reference to central terminals of zero and nonzero potentials Am Heart J 50 694
6 FRANK E & C F KAY 1953 A reference potential for unipolar electrocardiographic measurements on models Am Heart J 46 195
7 FRANK E 1955 Determination of the electrical center of ventricular depolarization in the human heart Am Heart J 49 670
8 BERRY P M & R H BAYLEY Boundary potentials due to a dipole in the oblate spheroid Unpublished observations
9 LABARTHE L F KOBOS & R H BAYLEY The impedance bridge for unipolar potential measurements due to a current dipole in homogeneous volume conductor of arbitrary boundary Unpublished observations
10 ECKEY P & R FROHLICH 1938 Zur Frage der unipolaren Ableitung des Elektrokardiogramms Arch Kreislaufforsch 206 181
11 BURGER R 1939 Über das elektrische Feld des Herzens I Mitteilung Cardiologia 3 56
12 DOLGIN M S GRAU & L N KATZ 1949 Experimental studies on the validity of the central terminal of Wilson as an indifferent reference point Am Heart J 37 868
13 MAXWELL J C 1892 A Treatise on Electricity and Magnetism 2 Oxford Univ Press London England
14 WILSON F N & R H BAYLEY 1950 The electric field of an eccentric dipole in a homogeneous spherical conducting medium Circulation 1 84
15 BAYLEY R H E W REYNOLDS JR C L KINARD & J F HEAD 1954 The zero of potential of the electrical field produced by the heart beat The problem with reference to homogeneous volume conductors Circulation Research 2 4
16 BAYLEY R H & C L KINARD 1954 The zero of potential of the electrical field produced by the heart beat The problem with reference to the living subject Circulation Research 2 104
17 BAYLEY R H & A E SCHMIDT 1955 The problem of adjusting the Wilson central terminal to a zero of potential in the living human subject Circulation Research 3 94
18 MCFEE R & F D JOHNSTON 1953 Electrocardiographic leads I Introduction Circulation 8 554
19 MCFEE R & F D JOHNSTON 1954 Electrocardiographic leads II Analysis Circultion 9 255
20 MCFEE R & F D JOHNSTON 1954 Electrocardiographic leads III Synthesis Circulation 9 868
21 FRANK E 1954 General theory of heart vector projection Circulation Research 2 258
22 FRANK E & C F KAY 1954 Frontal plane studies of homogeneous torso models Circulation 9 724
23 WILSON F B 1931 Vector Analysis Gibbs 7th ed Yale Univ Press New Haven Conn
24 MARCHAND N S BRILLER & C E KOSSMANN 1954 General networks for central terminals in electrocardiography and vector cardiography Circulation 12 838
25a BURGER H C & J B VAN MILAAN 1946-1947 Heart vector and leads Brit Heart J 8 157
25b BURGER H C & J B VAN MILAAN 1946-1947 Heart vector and leads II Brit Heart J 9 154
26 CHU L J 1948 Personal communication with R H Bayley
27 SMYTHE W R 1939 Static and Dynamic Electricity McGraw Hill New York N Y
28 STRATTON J A 1941 Electromagnetic Theory 175 McGraw Hill New York N Y

DISCUSSION PART V

G E Burch *Chairman*

E V NEWMAN (*Vanderbilt University School of Medicine Nashville Tenn*) I should like first to re-emphasize and extend two significant ideas expressed by Burger They may be a little philosophical, but they seem to me to be very pertinent First Burger implied that an investigator thinks he has things quantified when he really means he is only satisfied I should like to add that being satisfied is governed to a large extent by the purposes served by the quantification The point is the old one that one need not carry calculations out to five significant figures when two or three are satisfactory for the purpose Second Burger made the point that interpretation is always necessary whether the investigator is a physician physiologist or physicist For the physician, interpretation means correlation with other information from the history, physical findings and chemical and anatomical studies

Our approach to the vectorcardiographic representation has been to deal with the crude information directly We have made no corrections by lead vectors lead field corrections transfer impedance or skew factors of any type. Incidentally I hope someone will clearly set forth the relationships or differences between the expressions Burger vectors Schmitt s transfer impedance and Johnston s lead field correction

Making no allowances for skew factors or transfer corrections I have approached the use of vector leads in the following fashion Leads were placed on the patients according to what seems to be an externally orthogonal system used by W R Milnor The information from this reference frame (which is *not internally orthogonal*) was then *fed into a calculating* device (variously called a Schmitt resolver a panoramic unit or a vector aspect changer) This device automatically and instantaneously calculates or derives the scalar electrocardiogram that would be seen from any other reference axis within the orthogonal frame Comparisons could then be made between the derived scalar electrocardiogram on any axis and the scalar electrocardiograms taken directly from surface electrodes

My purpose was very simple and crude—in other words I should be easily satisfied My criterion of good comparison was merely whether the derived scalar tracings contained the information that I considered important in current practice Putting it more simply Could the same interpretations be made from the vector derived scalar electrocardiograms as were made independently from the routine surface leads?

How could all of us ever agree that the electrocardiographic scalar tracings derived entirely from three basic bipolar reference leads are adequate and accurate for interpretation? The only way I know is to show each individual several hundred examples of correlation The instrument (vector aspect changer) allows rapid exploration of all the derived scalar representations The ultimate advantage would be to reduce the electrocardiographic picture to three basic reference axes The translation of previous information and experience

into the new experience can be done with rapid electronic calculation In this regard Schmitt s device is a great help and an advance in methodology

Another type of quantification that has been discussed is the integration of the scalar electrocardiogram with vector addition of the integrals The concept of gradient has received further attention lately and more rapid methods of exploration of the concept are being devised One of the difficulties with the classical mean gradient is that it discards some information while synthesizing and simplifying other data Representing the gradient as a straight line having magnitude and direction leaves out one of the most important phases of the information namely time I notice that Briller finds it necessary to interpret the gradient in conjunction with the shape and direction of the vector loop presentation

The first step in representing the continuous spatial vector integral was to devise a method This has been successfully accomplished by my engineer, Thomas G Arnold The instrument Arnold devised will calculate continuously the integral of the scalar electrocardiogram and will add the integrals vectorwise The result is the vector integral cardiogram (VICG) The instrument includes an automatic system for starting and stopping the integration for each cardiac cycle at a preselected point in the T P interval This feature of the technique allows us to compensate for base line shift or wandering which has been a serious obstacle to obtaining accurate integrals Time markings on the VICG with the direction indicated by intensity modulation of the beam complete the information

With the vector aspect changer and continuous integrator one can easily and rapidly compare derived scalar electrocardiograms from any reference frame with actual surface leads and can demonstrate the continuous formation of the gradient (VICG) from cycle to cycle Examples of this technique have been given in previous publications [1, 2, 3]

References

1 Milnor W R A Genecin S A Talbot & E V Newman 1951 A vectorcardiographic study of the Q_3 deflection in cases of myocardial infarction and in normal subjects Bull Johns Hopkins Hosp 89 281

2 Milnor W R S A Talbot & E V Newman 1953 A study of the relationship between unipolar leads and spatial vectorcardiograms using the panoramic vector cardiograph Circulation 7 545

3 Newman E V 1955 The important recent advances in electrocardiography A M A Arch Internal Med 96 591

H K Hellerstein (*University Hospitals Cleveland Ohio*) I should like to raise the question of the advisability of applying the present somewhat imperfect knowledge to clinical problems today without correction of skew and other factors There are two possible viewpoints regarding this application One that of the purist would be to restrict the vectorcardiogram to theoretical investigation only and to use it clinically only when *all* factors have been resolved quantitive aspects skew factors and other relationships that have been so well discussed in this monograph The second viewpoint involves the acknowledgment of deficiencies the correlation of the imperfect facts with previous knowledge experience and experiments and the clinical application

of this information The latter view recognizes the value of imperfect data If in the past fifteen years the purist view had produced precordial leads whose values were now indisputable, they would not have been employed until the differences between the Wilson central terminal and the various limbs as in different electrodes had been determined

We may properly raise the question as to whether the use of vectorcardiography is urgent today since the same information can be obtained by the use of simultaneously recorded scalar electrocardiograms I believe there is a clinical need for simplification of the function of the heart station In the University Hospitals of Cleveland we take sixty to eighty electrocardiograms a day in addition to pulse tracings heart sound recordings and ballistocardiograms It is time consuming and expensive to process mount and interpret such voluminous material this impracticability gives promise of increasing in coming years If the information were available in the form of x y z components that is the vectorcardiogram could not the same information be obtained more readily? I believe that with the improved techniques now available for the clear presentation of the component parts of the vectorcardiogram (P QRS T) clinical interpretation can be simplified[4]

While recognizing the theoretical importance of clarifying the reasons for differences between the various reference systems I believe it is important to stress and to take clinical advantage of their similarities In studies comparing the vectorcardiogram obtained with the equilateral tetrahedral system and with the cube reference system I have been struck by the remarkable similarities in the component major vectors in their timing and in the general spatial orientation with predictable differences relative spatial magnitude and relative spatial velocity

Figure 1 is a representative example demonstrating that identical information is present in both systems In the upper row where the tetrahedral reference system is employed one notes that the initial portion (0 to 0 026 sec) of the isolated QRS of a patient with posterior infarction is directed cephalad rightward and ventrally while the second portion (0 056 sec) is directed cephalad leftward and dorsad The loop is open with the junction vector directed rightward and ventrad The same basic information is present with the cube system (lower row) These similarities obtain for the isolated P and T vector loops

In a comparison of the two systems in over a hundred subjects the differences have been systematic and quite predictable related for the most part to the greater proximity of the left arm Thus far we have found no instance with discrepancies of the type presented by Burger that is in which there is a disparity of 180 in direction When the plane of the loop is approximately perpendicular to a plane slight differences in the placement of the reference electrodes could effect a change of the direction of inscription for that plane This difference however probably is not significant

Consonant with the concept that the similarities of the tracings obtained with different systems from a clinical viewpoint outweigh the dissimilarities is the observation that the spatial loop is altered insignificantly by changes in the position of the body

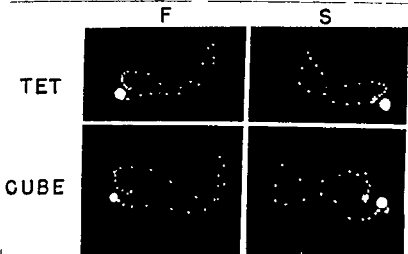


FIGURE 1

In a comprehensive study of representative heart diseases we have found that the direction of inscription the basic configuration the interrelationship of component major vectors and the form of the spatial magnitude and spatial velocity electrocardiograms did not change The same clinical diagnoses were apparent in the various postures FIGURE 2 is a representative example

The quantitative changes might dissatisfy the rigid tolerance of the pure scientist but not those of the clinician

I have referred to the spatial magnitude and spatial velocity electrocardiograms that I am studying currently in man and dog The spatial magnitude electrocardiogram has been alluded to by Abildskov and was first studied in 1955 by Sayers[2] The spatial magnitude electrocardiogram is a new transformation method for studying the cardiac electrical activity and consists of the calculation of the total resultant spatial magnitude of the equivalent cardiac vector as a function of time[2]

The spatial velocity electrocardiogram is an entirely new and as far as I know previously unpublished method for studying the heart s electrical activity The spatial velocity electrocardiogram may be approximated by inspection of the distance between the time interruptions of the spatial loop and by calculation of the change in spatial angles and magnitude between consecutive vectors

$$SV = \sqrt{\left(\frac{dx}{dt}\right)^2 + \left(\frac{dy}{dt}\right)^2 + \left(\frac{dz}{dt}\right)^2}$$

or by an analogue computer currently in construction

The forms of the spatial magnitude and spatial velocity electrocardiograms in the two systems mentioned above remain remarkably similar

I should like to suggest that while the skewness and other factors are being

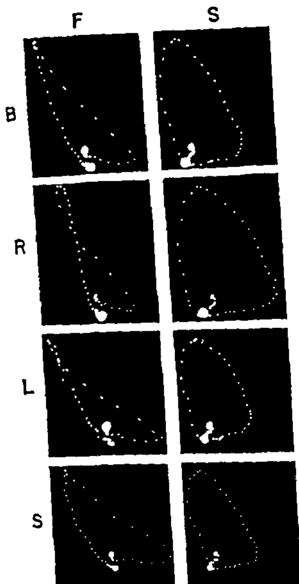


Figure 2 QRS vector loop of patient with proved anteroseptal infarction right bundle branch block and right ventricular hypertrophy in four postures B (back) R (right side) L (left side) and S (sitting)

derived there should be a wider clinical application of vectorcardiography because of its ease of application because of the economy in taking the records especially in busy hospitals and because the same and even additional information is obtained more readily

References

1 HELLERSTEIN H K D SHAW & T SANO 1954 Dissection of the vectorcardiogram differential vectorcardiography Am Heart J 47 887
2 SAYERS B McA F C SILBERBERG & D F DURIF 1955 The electrocardiographic spatial magnitude curve in man Am Heart J 49 323

E SIMONSON (*University of Minnesota Minneapolis Minn*) It is logical to apply the principles of spatial vectorcardiography to the measurement of electrocardiographic intervals In conventional electrocardiography intervals are measured as the longest in any single limb lead but this is only a crude approximation since the initial or terminal segment of the spatial loops may not be fully projected on any single limb lead or on the frontal plane as a whole H Blackburn and I measured the spatially correct QRS duration from three orthogonal leads one horizontal lead (right to left midaxillar line at the level of the fifth interspace in the midclavicular line) one vertical lead Y (head to Y_2 position in the same horizontal plane) and one sagittal lead *Z* (in V_1 position at the same horizontal plane and an anatomically opposite point on the back) A fast speed two channel jet writing machine with a galvanometer sensitivity of 500 cps was used One channel was used for the timing reference and the QRS duration was determined as the difference between the earliest and latest deflections of the QRS complex in any of the leads X Y or *Z* These leads are anatomically but not ideally orthogonal electrically However they approach electrical orthogonality as recent studies by Schmitt and ourselves have determined and they appear to be sufficiently accurate for interval measurements

In 115 healthy men from 20 to 50 years of age the spatially corrected QRS duration ranged from 0 0801 to 0 1309 sec with a mean of 0 1010 sec and a standard deviation of 0 010 sec There was only a slight skewness in the frequency distribution of the sample As expected both the lower and the upper limits exceeded significantly those QRS durations obtained from conventional measurements There was a significant correlation with the QRS interval measured from the frontal plane limb leads but the correlation was too low for individual prediction of the true QRS interval from the conventionally determined QRS interval On the basis of the frequency distribution an upper normal limit of 0 12 sec is proposed There was no correlation between the heart rate and the QRS interval in the range corresponding to an *R R* interval from 0 7 to 1 1 sec but there was a highly significant negative correlation at slower or higher heart rates There was no correlation between the QRS interval and body weight or age It is expected that spatially corrected interval measurements will improve the differentiation between the normal and the abnormal in clinical electrocardiography

H SCHAEFER (*University of Heidelberg Heidelberg Germany*) I should like to explain a method of vector analysis that we developed some years ago in Heidelberg Germany At an appropriate point of the cross section of the thorax we assume a dipole center and draw lines from it to every electrode point On these lines the absolute amount of the potential recorded with this special electrode is plotted starting in the dipole center The perpendicular is

erected at the top of the potential All perpendiculars should cross at one and the same point the spike of the resulting potential vector In fact the perpendiculars cross at very different points but it is possible to construct a circle to which all perpendiculars are either tangents or secants This circle is named the circle of error It gives a fairly good picture of the probable point at which we may find the position of the integral vector If we make certain shifts of the dipole center the diameter of the circle of error changes but fortunately the position of the resultant vector is only very slightly shifted This has given us some feeling of optimism concerning the applicability of a vector analysis

H C BURGER (*University of Utrecht Utrecht The Netherlands*) I must congratulate Schmitt on his method and results The relation of the coefficients to the dipole depends on many variables Schmitt s treatment of this problem will certainly clarify the situation with regard to the human body

I should like to mention another point on which I cannot entirely agree with Schmitt It involves the question of whether we have a voltage or a current dipole in our body I think that this is just a question of words When we try to define the shape of a vectorcardiogram I think Schmitt will agree that it does not matter at all

O H SCHMITT (*University of Minnesota Minneapolis Minn*) I do not agree

H C BURGER It depends upon the ideas we have about the vector

O H SCHMITT No I contend that while both current and voltage dipoles *exist* in the body fundamentally different assumptions underlie the choice of one or the other as a source variable While electrically correct mathematical analyses can be carried out on the basis of either variable these two analyses differ considerably in their convenience and results and cannot conveniently be translated one into the other

H C BURGER When we want the absolute value we multiply one value by a factor to obtain the other This factor should not be called the impedance Some other name should be used

When I saw the words zero potential between quotation marks in the title of Bayley s paper I felt satisfied This satisfaction disappeared however when I saw that within the paper he used the words without any trace of those quotation marks I think we should remember that there is no such thing as an absolute zero of potential We can connect any point on the body with ground and consider this to be zero potential This question is related to the notion of the mid potential as the average value of two poles A dipole is not two poles however but is one singularity Even if we have two poles the potential of either pole depends on its magnitude and shape In the ideal case of two point poles the potential is infinite *one pole being positive* and the other negative In either case I do not see the significance of the mid potential

With regard to the error of the Wilson central terminal we could take averages of potentials of many different places on the body just as we take the average of potential of both arms and a leg We can ground the central point even so however its potential is not zero but changes with time I do not see therefore how we can speak of an error

O. H. Schmitt: With reference to the presentation Burger has offered, and pertinent to Katz's introductory remarks, it seems that several theoretically establishable points have been misunderstood or have remained unnoticed. These can be brought into focus for critical consideration by performing "thought experiments," that is, illustrative experiments that need hardly be performed in actuality because their results can be predicted with confidence.

First, there has been considerable discussion in the literature of "good" and "bad" electrocardiographic leads, generally in reference to such factors as the uniformity, the orthogonality, and the local selectivity of the lead. Let us suppose that it might be possible to specify leads that are exactly constant in transfer impedance throughout the heart region. These leads, now technically not too far from realization, would be excellent from the point of view of the investigator anxious to achieve a true weighted integration of all heart sources, but they would be very poor from the viewpoint of localization. Inverting the procedure by which nicely orthogonal uniform leads are obtained, it is possible by utilizing what is called a "gradiometer" connection of leads to achieve highly nonuniform sensitivity of recording, either in a radially divergent or in a relatively uniform nonlinear pattern. Ordinarily such a gradiometer connection yields an approximate inverse cube sensitivity, but a higher power discrimination, limited only by intrinsic noise, is easily incorporated. These systems would be very desirable in the sense of localization but undesirable for uniform recording. If we separate our thinking with respect to these two quite divergent goals of "goodness," we shall experience less confusion with respect to the assessment of leads.

Second, it seems important to differentiate sharply between current dipole sources and voltage dipole sources in applying electrical superposition theory to the summation of physiological action potential contributions from various regions of the heart. While careful mathematical analysis produces a correct conclusion, reasoning either in terms of voltages or currents, there is error in the usual sophomore physics notion that voltage sources must sum if equivalent current sources so do, because current and voltage are related by a constant through Ohm's law in simple linear circuits.

It is possible to illustrate this point in a sophisticated manner for a continuum of conductivity with distributed sources, but for our purposes the following simple example will suffice. Consider the rudimentary electrical mesh shown in FIGURE 1. Suppose all resistors in this diagram to be of unit value, terminal pairs AB and CD to be points where sources are applied, and EF to be an output at which the resultant contributions are to be measured.

Suppose that a potential difference of 5 v. is applied at AB and that the output EF is measured. A simple calculation will show that 1 v. may be expected at EF. Now suppose that a potential difference of 3 v. is applied to CD. There will now be an output of 3/4 v.

Naive utilization of the superposition theorem might fallaciously lead us to expect 1 3/4 v. at EF when both sources are applied additively. We should find only 1 v. for the combined sources, however, proving that the output is identical whether or not the input to CD is connected.

Correspondingly, voltage produced in the heart by one muscle bundle may

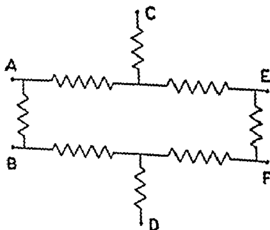


Figure 1

be completely masked in its effect by voltage from another bundle when both are active but would be evident when the first bundle was active alone

For current sources the superposition theorem does apply very simply Had we applied *currents* of 5 and 3 amp respectively to AB and CD we should have found a potential at EF of $^5/_6$ v for the source at AB and of $1^1/_2$ v for the source at CD and with both a voltage of their sum or $2^1/_3$ v

On this basis it seems important to think of action currents rather than action potentials as the additive contributions from individual fiber bundles to the measured surface potential Dimensionally the ratio of an output voltage to an input current must be an impedance and consequently this proportionality constant is named transfer impedance

Finally it seems important to de-emphasize the search for a physiologically ideal zero potential While it is perfectly true that for formal integration of electrostatic field patterns it is often important mathematically to choose a zero point that simplifies the procedure there is nothing very important physically about this particular potential and it can often be chosen in several different ways with equal convenience For a dipolar current source it is esthetically pleasing to choose the equipotential that has symmetry with respect to that source as an origin and this is generally done

In the case of the heart there is no place in the cardiac region even approximately equipotential with any of the zero potentials or central terminals even those very elaborately developed with many electrodes Thus even the best zero potential approximates only the symmetry potential for that part of the dipole distribution that can be regarded as lumped

H C Burger What is the aim of vectorcardiography? What can vectorcardiography give us that we cannot already achieve with electrocardiography? I believe that the final aim of vectorcardiography is practice Toward the achievement of this end there are several points to be considered One involves phase differences As a rule they are neglected in scalar elect

grams Of course they can be taken into account but this is not sc we have two curves recorded one below the other While vecto gives us nothing new it does provide an easy means to visualize differences This is merely an intricate mathematical deduction h contend that information is not gained by mathematical proof i have its meaning and so it is with vectorcardiography Our brain tioned to see shapes and not curves Vectorcardiography presents i us in a new form and makes it possible for us to see curves thus er learn more rapidly, with a corresponding lessening of the chance With this in mind we should be able to say that vectorcardiography its place in medical practice not as a replacement for electrocardiogra as an adjunct to it

C E Kossmann (*New York University New York, N Y*) I think another point that possibly we are overlooking and that is What are w to do with the vectorcardiogram? Are we simply trying to look at its make deductions as we have done with the scalar electrocardiogram trying to measure some parameters in the vectorcardiogram that measurable or not easily measurable in the scalar electrocardiogram will of course determine whether we shall eventually use vectorcar *and the type of reference frame that will be used*

I N Katz (*Michael Reese Hospital Chicago Ill*) I think the argumer is a question of what is empirical and what is scientific If we go i whole of electrophysiology of the heart in relation to the volume conc the zero potential or the stereovectors it seems that the problem is alw same if it is yours it is scientific If it is that of someone else it is emp

There are not many of us who create universal truths and ignore dev It is given to only a few to recognize that the errors introduced by the concepts are not too important There are others of us who are pur who are so overwhelmed by the deviations that we fail to see the unive In other words we might say that something is 85 per cent correct or we say it is 15 per cent in error depending upon how we use it to express our point I wonder whether many of our differences are not based on just attitude

Are there unipolar leads? To me the concept of unipolar leads would that the second electrode is truly indifferent and that it does not vary the heart cycle I think that what troubled Burger and troubled me was too many times zero potential with or without quotes was incorrectly i What was really meant is that during its cycle the heart does not appreci influence one of the electrodes that the electromotive force of the heart nothing to do with absolute quantity or grounding values

Bayley s paper calls to my mind a time when we had a swimming pool at Michael Reese Hospital in Chicago and we put some interns into it thought we had obtained some truly nonvarying indifferent potentials must admit that I am overwhelmed by Bayley s analysis I am not c whether the use of a plastic belt or submersion in a bathysphere, or

similar technique is the answer The physicists and those who like Bayley have studied the problem diligently should get together and the rest of us should wait with bated breath for this decision

I should also like to know whether there are proximity effects Is it sufficient to obtain vectors or stereoscopic vectors, or should we worry if we do not record a series of chest leads? Might we not miss information obtained from electrodes placed on the anterior chest wall the esophagus, or elsewhere that might become lost in the shuffle because it would be so overwhelmed by the rest of the information? I raise this question in the face of the tendency to supplant scalar electrocardiograms by vectorcardiography I must admit however, that during the many times I have heard Schmitt present his material I have had the feeling that if you are not sophisticated in electrocardiology by constant practice perhaps orthogonal lead systems may be an easier way to obtain the same information I am quite willing to agree to this But before we do it at the Michael Reese Hospital I should like to know which combination we should use I am told that there are three good leads and a dozen bad lead combinations and depending upon our source of information we come to a different decision of which is good and which is bad

I recall that when the chest leads came in we used a connection that was upside down Then Wilson fortunately came along and changed it He said it must be the V not CF or CP Wilson knew that the central terminal was not indifferent and we agreed to use it although it was not perfect Perhaps the day has come to begin to think in terms of orthogonal leads even without the perfect system they may not replace the conventional methods but we should persuade a new generation to think in terms of x y components with or without correction factors In another twenty five years perhaps we shall have something less empirical and more informative

Finally however when we get such orthogonal leads we shall have no more real insight into what happens in the heart than we had before but we shall have an integration of an infinite number of leads and this will be an advantage